H Y P N O T I C S.

WITH SPECIAL REFERENCE TO THEIR USE IN MENTAL DISEASE.

Being a Thesis for the Degree of M.D.

b y

BERNARD RAMSAY CRAIG CHRISTIE,

M.B., C.M., Edin. Univ. (1897)

late

Assistant Medical Officer, Gartloch Asylum;
and Hospital Non-resident Clinical Clerk,
Royal Edinburgh Hospital for sick Children;
& Resident House-Physician and House-Surgeon,
Glasgow Royal Infirmary.

--------ooOoo--------

"When I lie down I say, When shall I arise and the night be gone? and I am full of tossings to and fro unto the dawning of the day."

JOB. VII. 4.

C O N T E N T S.

Chapter I.

Introductory - Sleep and Sleeplessness - Causes of Sleeplessness - Their Classifications - Its treatment without Drugs - By Mechanical Appliances - Hypnotism and Suggestion - Massage and Electricity.

. . . . . .

Chapter II.

HYPNOTICS.

Group I.

Paraldehyde - Amylene-hydrate - Amylene-chloral.

Group II.

Sulphonal - Trional - Tetronal.

Group III.

Chloral - Butyl-chloral Hydras - Chloralamide - Chloralimide - Chlorobrom - Chloralose - Chloral-urethane or Ural.

. . . . . .

Chapter III.

HYPNOTICS (Continued)

Group IV.

The Bromides - Cannabis Indica.

Group V.

Opium and its alkaloids - Hyoscyamus and its alkaloids.

Group VI. (Miscellaneous)

Alcohol - Urethane - Somnal - Hypnone - Methylal - Hypnal - Piscidia - Pellotine Propione - Antipyrine - Phenacetin - Lactophenin - Chloroform - Duboisine - Monobromide of Camphor - Lupulus - Sumbul - Musk - Boldo-glucine - Boldin - Chamomile Flowers - Dover's Powder - Digitalis - Turpentine - Water - Milk - Lettuce.

. . . . . .

INDEX OF REFERENCES.

(At end)

CHAPTER I.

INTRODUCTION.

"I wish I could write a chapter upon Sleep; it is a fine subject."

"Tristam Shandy".

Among the many and varied subjects which one has to choose from in writing a dissertation, it seems to me, that that subject which the writer is most familiar with, must always appear - at least to him - to be the most interesting; and therefore the one to which he will generally direct his best efforts.

It happened to me, that, immediately after my graduation, I was appointed Resident Assistant Medical Officer to Gartloch Asylum and Hospital for Mental Diseases, which is one of the most modern asylums in the West of Scotland, and has accommodation for upwards of 600 patients.

During my tenure of office there I became much interested/

interested in that great problem which besets all asylum physicians, namely, how to deal with Sleeplessness; such a question presents itself to every one engaged in practice, but I venture to think that it lends itself more especially to those engaged in the treatment of Mental Diseases, and therefore in writing on Hypnotics as the subject of my Thesis, I would specially direct attention to their use in asylum practice.

The literature on this subject is becoming more extensive every day; one can scarcely pick up a medical paper which does not give an account of some new remedy which has just come out, and which is designed to surpass all previous ones in procuring Sleep. But, alas, the perfect hypnotic, like the Philosophers Stone, has yet to be found.

Many and varied are the different forms of sleeplessness which call for treatment, and we are all familiar with the numerous little devices which are practised - some of them successfully enough - in order to woo Nature's sweet nurse. There are those who read themselves to sleep or count imaginary sheep jumping through a hedge, and some, like Southey, find repose in thinking of some monotonous discourse.

But/

But these lesser forms of insomnia need not detain us here, for they seldom require the aid of the physician, and I now pass on to consider its more serious aspect. In dealing with this subject, I have not hesitated to quote freely from the opinions expressed by others - from their researches on the subject - and in so doing, have endeavoured to present to the reader a clear and succinct account of the relative values of each of the drugs described.

I would mention that all of the more important hypnotics which I describe, have been used by me on very many occasions, and that I was nearly always my own dispenser. This latter fact is, I think, of great importance; for besides observing their therapeutic action, nothing can familiarise one with drugs more than having to dispense them oneself; and as in an asylum the patients can be visited at any hour of the day or night, the effects of an hypnotic may always be most particularly noted.

It is perhaps hardly necessary for me to point out that accurate dispensing is of primary importance, and next to that, the sleeping-draught should always be rendered as palatable as possible, the more especially/

especially when it is given to the insane.

However, before passing on to the consideration of Hypnotics, which however harmless they may be said to be, must always remain as the last resort of the Physician; I would briefly consider sleep and sleeplessness.

No one will deny that of all the great blessings of which man is heir to, sleep is one of the greatest. How many a toiler looks forward to that portion of the twenty-four hours, when all nature is lulled in sweet sleep and all cares are forgotten, which Virgil has so poetically described in the AEnied.

> "Nox erat, et placidum carpebant fessa soporem
> Corpora per terras, silvaeque et saeva quierant
> AEquora, quum medio volvuntur sidera lapsu,
> Quum tacet omnis ager. Pecudes pictaeque volucres
> Quaeque lacus late liquidos, quaeque aspera dumis
> Rura tenent, somno positae sub nocte silenti,
> Lenibant curas, et corda oblita laborum." (1).

We read that the ancients had a special god of sleep, Somnus, whose son Morpheus, was the god of Dreams, and we may be sure that these two were not the least of their deities in heathen mythology.

The nature of what sleep really is, is ill understood, and is a question which physiologists have as yet to fully answer; and as long as the physiology of sleep is unknown, its pathology must remain unknown also.

Insomnia/

Insomnia is not a disease, but it is to be regarded as a symptom and one that is of considerable importance. In speaking of it, I purpose to consider its treatment, 1st without drugs, 2nd, with drugs; the former I will just briefly indicate, for it does not concern my present purpose; the latter, which deals only with hypnotics, is really the subject of this thesis, and accordingly it will be treated of at considerable length.

The varieties and causes of insomnia have been variously classified. Germain See recognises nine divisions, which are as follows:-- (1) Dolorous; (2) Digestive; (3) Cardiac & Dyspnoeal; (4) Cerebro-Spinal & Neurotic; (5) Psychic; (6) Insomnia of cerebral and physical fatigue; (7) Genito-urinary; (8) Febrile; (9) Toxic.

I mention this classification as it seems to me to be most complete and suggestive, but I think it will be found better for my present purpose, to be less ambitious and adopt a shorter one. That adopted by Bradbury(2) in the Croonian Lectures which is essentially the same, divides the causes of insomnia into four varieties; and in considering these separately I will briefly indicate their treatment.

1. Irritative Causes:

Here we have these cases in which insomnia is caused by pain, as in toothache, abscess formation, injury/

injury, the irritation produced by worms - so frequently observed in children - itching, as in some skin diseases, vesical irritation, coughing, noise, etc. The treatment resolves itself into removing the cause in so far as that is possible and the application, if necessary, of hot and cold fomentations, poultices, etc. Where the pain is caused by a surgical operation or injury, etc., opium in some of its many and varied combinations may be advantageously given.

II. Toxic Causes:

Here the insomnia is produced by the irritation of some toxic influence on the system, as in alcoholic indulgence, indigestion, gout, fevers, where the extreme restlessness is often one of the chief discomforts. As regards treatment each individual case must be treated on its own merits. In cases of fever, tepid sponging and warm baths, hot drinks, the exhibition of antipyretics, are all of the utmost value.

III. Physical Causes:

Are when insomnia arises from such causes as shock, extreme grief or joy, mental worry, business cares, etc. We all recognise these as common causes of insomnia, from which no one is exempt. Shakespeare(3)has ably portrayed this state of matters in

King/

King Henry IV., when he makes the king, tossing restlessly on his bed, soliloquise:

> How many thousand of my poorest subjects
> Are at this hour asleep - Sleep, gentle sleep,
> Nature's soft nurse, how have I frighted thee,
> That thou no more wilt weigh my eyelids down,
> And steep my senses in forgetfulness?
>
> * * * * * *
>
> Canst thou, O partial sleep! give thy repose
> To the wet sea-boy in an hour so rude;
> And, in the calmest and most stillest night,
> With all appliances and means to boot,
> Deny it to a king? Then, happy low, lie down!
> Uneasy lies the head that wears a crown.

IV. Change in mode of life:

For example, the first night in a strange house, eating of late dinners by those unaccustomed to them, the insomnia caused in nurses by changing from day to night duty - conditions which all in due time, generally correct themselves.

Before leaving the subject of the treatment of insomnia without recourse to drugs, I should like to just briefly speak of three forms of treatment which have in certain cases of sleeplessness been found efficacious.

1st. Treatment by Mechanical Appliances:

These are many and various, and include rocking beds, etc. One of the most recent is that invented and patented by Mr John H. Walker. This is a bed which has been extensively tried and favourably/

favourably reported on in several of the leading infirmaries. It was in use at Gartloch Hospital and I am quite familiar with it. Its outstanding feature is an automatic rhythmical movement which is entirely under the patient's control, and by which his whole body is alternately raised and lowered into the horizontal position, the bed is worked in connection with the water supply of the house and is arranged so as to be perfectly noiseless in its action. It was tried in the Edinburgh Royal Infirmary in the wards of the late Professor Thomas Grainger Stewart and Dr Gibson says at the close of a notice in the Lancet(4) "In many neurotic affections it has been found to produce beneficent results, more particularly in cases of insomnia and restlessness. It has, moreover, been of use in digestive, circulatory and respiratory troubles."

Speaking for myself, I feel that I have not as yet had sufficient experience of the bed, to give it a fair trial; but from what I have seen of it, I believe that it will be found of the utmost value in many of these neurotic cases which are often so difficult to treat.

2nd. Treatment by Hypnotism, Suggestion, etc.

Personally, I have no experience of this form of treatment and have never used it; those who advocate its use, speak highly of its efficacy. It is/

is said to do best with the neurotic; but surely these are the very class of patients on whom it ought not to be used. The remedy is undoubtedly a dangerous one, and one that should only be used by those of unquestionable experience. The young practitioner will do well to fight shy of it, for many have practised it only to bring discredit on the profession and opprobrium upon themselves.

Dr Alexander Robertson of Glasgow at the last meeting of the British Medical Association in Edinburgh, strongly advocated the employment of what he called "Psychic Suggestion", which is simply treatment by suggestion without, however, putting the patient in the hypnotic state. It is certainly remarkable what can be accomplished by suggestion alone. I have frequently observed, both in the sane and insane, that sleep is often easily induced by the physician simply assuring the patient that after he has taken, let us say, a hot drink, and settled himself for the night, that he will begin to feel sleepy in the course of half an hour or so, and will soon be asleep. And frequently he does go to sleep as if by magic. Is this "Suggestion"? If not, what is it? But I fear this subject is too much involved to allow of me discussing it further in this dissertation.

3rd. Treatment by Massage & Electricity.

Lastly, the employment of the two above methods of treatment in suitable cases, has frequently given good results.

In speaking of the hypnotics, I have arranged them in six groups, in what I consider is the relative value of their usefulness in asylum work. Generally speaking, I have found this classification - though it is necessarily somewhat artificial - to be one of the best in practice.

CHAPTER II.

HYPNOTICS.

Group I. Paraldehyde and Amylene Hydrate.

Paraldehyde ($C_6H_{12}O_3$)

A product of the polymerisation of Aldehyde by various acids and salts. This is a colourless liquid with a penetrating ethereal odour and a burning taste. Dose: ½ - 2 Fluid Drachms.

This drug was introduced into practice by Cervello of Palermo about the year 1883. It is certainly one of the best hypnotics which we have in insanity. From its very rapid action, its stimulating effects, and the sound sleep which it induces, with absence of after bad effects, it is to be regarded as a powerful and valuable hypnotic.

It is most useful in procuring sleep, especially where a stimulant action is indicated, as in the insomnia of Dementia and Melancholia, and in the restlessness and excitement of Mania, where the cardiac action is often weak.

I have given it very frequently, never in doses of less than two drachms at a time.

In cases of very acute excitement, when the patient could not be left to himself for an instant,

I/

I have given as much as four drachms of Paraldehyde combined with forty-five grains of Bromide of Potash - an excellent combination - and then got the patient to bed in a quiet room, with the blinds drawn. Sleep very soon ensued, sometimes in a very few minutes, and continued for about eight hours, the patient awaking refreshed and the excitement quite subdued.

From my own experience in these cases, I think that it is seldom necessary to resort to the stomach-tube in order to administer the sleeping-draught; patience and a little coaxing on the part of the medical attendant will nearly always succeed.

The taste and penetrating smell of paraldehyde are certainly not in its favour; and in this respect it is inferior to Amylene Hydrate; for though the breath is affected for many hours after its (amylene hydrate) administration, the odour is not nearly so offensive as in the case of paraldehyde. I have always found it most easily given when mixed with some orange syrup and swallowed with a draught of water at bedtime.

Clouston[1] speaks of it as acting well when given by the rectum.

Paraldehyde is, I think, of special service in the mania of alcoholic insanity or delirium tremens: and in such cases it is highly recommended by Goodhart/

Goodhart.[2] It is well borne, and I have given it in doses up to four drachms. It has the great advantage of warding off heart failure - a not uncommon termination to such cases. But I would mention that it has in a very few cases in which I have used it seemed to increase the mania on awakening from sleep. And in this respect Bevan Lewis[3] speaks disparagingly of it.

Whitla[4] refers to it as resembling Chloral in its action, but without its depressing effects; and describes it as being a pure hypnotic, diuretic, but not diaphoretic in its action, and affecting the cerebral cells, and in poisonous doses the respiratory centre.

Gordon[5] has shown that even in minute doses it aids the peptone-forming power of pepsin, accelerating the digestion of Fibrin. This last is a fact of considerable importance, for I believe few hypnotics have this property.

I think it should be used with caution in cases of adolescent mania as it is undoubtedly a powerful stimulant to the sexual organs and may increase in these cases habits of masturbation as I have sometimes observed.

With regard to its toxic effects, Clouston[6] relates a case where by mistake the patient, a small sized woman in weak health, received an ounce in/

in one dose, with the result that she slept a stertorous sleep for twelve hours, the heart's action not being interfered with. Rousing and coffee on several occasions during the night only very partially brought her to consciousness while under its influence. She seemed none the worse afterwards.

I remember on one occasion giving two drachms of Paraldehyde to a melancholic patient who had been troubled for some time with severe attacks of Asthma, and could get no rest. In this case the drug did not act well. The patient, who was bronchitic, did not get any relief from the asthmatic seizure, and the lungs the following day began to get "water-logged", the patient dying twenty-four hours after its administration. Though I cannot think that in this case the fatal issue was in any way accelerated by the paraldehyde, it has since seemed to me that the drug is contra-indicated in these cases where there is any respiratory affection.

On consulting the literature on this subject, a case is reported by Rolleston (7) of a woman with chronic emphysema who, after receiving a small dose of paraldehyde (one drachm) became very much collapsed, remaining very blue and breathless for some hours. Some days afterwards - her alarming symptoms at the time not having been attributed to the administration/

administration of the paraldehyde - she again received a similar dose; with the result that the previous symptoms again returned as before. After this, the drug was discontinued in her case.

A lethal dose of paraldehyde acts by suspending the functions of the medulla and respiratory centre, the heart ceasing afterwards.

On the other hand the use of Paraldehyde in Asthma is recommended by Bradbury[8] who says: "It is specially serviceable in this affection," and Goodhart[9] remarks: "It is a drug of unquestionable value in the restlessness and cardiac asthma so often seen in aortic disease, and in the labouring dilated heart of chronic Bright's disease."

There would thus seem to be some difference of opinion as to the relative value of this drug, where there is any respiratory affection. Small doses such as 10 or 15 minims seem to be relatively safe. But taking into consideration the fact that larger doses such as one drachm and upwards, have in a few reported cases, where there was respiratory weakness, shown a toxic effect, I think in this connection the use of the drug is not to be recommended.

With regard to its cumulative action, I have not observed this. And I think if the drug is administered well diluted and its use not continued too/

too long, that there is no cumulative action and a "Paraldehyde habit" does not tend to be established.

Indeed the "paraldehyde habit" is seldom formed by patients taking this drug, for its disgusting taste and smell, and the manner in which its odour clings to the breath, make it very disagreeable and an hypnotic whose use is not likely to be abused.

Savage[10] remarks: "In my experience there does not appear to be any cumulative effect; but on the other hand, patients soon get used to it, and the dose has to be increased." Paraldehyde has no analgesic action and in this respect is inferior to Opium. It is said to be very irritant to mucous membranes and to impair the digestion. Nasal ulcers, skin eruptions, and delirium are all reported to have followed its use. I have not observed any of these unpleasant effects myself, and indeed they seem to be rare. If the dose is well diluted there seems to be little danger of any irritant action.

On the heart its stimulant effect is most marked, in this respect resembling the primary effects of alcohol.

Wood[11] remarks that "It appears to have very little effect upon the circulation, though it has been shown by Quinquand that after large doses there is lessening of the heart force. In poisoning by it/

it the bodily temperature falls, the elimination of Carbonic acid is lessened and the colour of the blood is changed."

It is worth noting in speaking of this drug to mention that Dujardin-Beaumetz[12] thinks that it is specially indicated in strychnine poisoning, and speaks well of it in the treatment of eclampsia.

Paraldehyde has no diaphoretic action, its channels of excretion are confined to the kidneys and lungs. Though diuretic in its action, it does not very greatly increase the flow of urine. Its odour may be detected in the urine of patients, showing its very stable nature in its passage through the system.

With regard to the latter mode of excretion, it seems to be largely given off by the lungs. It is remarkable how long its odour lingers about the breath of those who have taken it, even for days afterwards. This is undoubtedly greatly against its use in private practice. It has never seemed to me that there is any advantage to be gained by combining paraldehyde with other drugs, except in the case of the bromides, where it seems to combine very well - otherwise it is best given by itself.

Briefly/

Briefly, its advantages may thus be indicated:-

(1) Quickness of action. There is no period of excitement before its hypnotic effect is produced.

(2) Safety in action - except in some cases where there is respiratory disorder, as previously indicated.

(3) Production of sound sleep. A dose of two drachms, or even less, generally causing eight hours sleep.

(4) Complete absence of after bad effects; except for odour in the breath.

(5) No constipating effects; indeed, it is said to be sometimes slightly laxative in its effects.

(6) Stimulant to the heart's action.

(7) No confusion of intellect following its use.

(8) In the large majority of cases, no loss of appetite or interference with the digestive functions.

(9) No weakening effects produced.

(10) "Paraldehyde habit" does not tend to be established.

Amylene Hydrate (Tertiary Amylic Alcohol, or Dimethylethyl Carbinol $(CH_3)_2 C_2 H_5 COH.$)

This substance is prepared by treating Trimethylethylene Amylene with Sulphuric acid and subsequent decomposition of the Amylene Sulphate with alkali.

It is a clear colourless oily liquid, with a somewhat ethereal odour, not unlike Paraldehyde, and is/

is fairly soluble in water. Dose 50 to 70 minims.

The physiological properties of amylene hydrate were first discovered in 1885 by Von Mering and Thierfelder. According to the former it is a valuable hypnotic, which takes a place midway between chloral hydrate and paraldehyde, one drachm of chloral, two of amylene hydrate and three of paraldehyde being about equivalent in power.

I believe from my own experience of this drug, that it is an hypnotic of considerable value; it is of comparatively recent date and is not officinal.

Its taste and odour are not nearly so strong as that of paraldehyde; and on this account, it is much more easily given.

It may be administered in capsules or by the rectum. I have always used it well diluted and shaken up with water, and the many patients to whom I have given it, seemed to find little difficulty in taking it in this form.

Though given off by the lungs, the odour is not nearly so offensive nor does it last so long as that of paraldehyde. It has no analgesic properties, and large doses are said to paralyze the medulla oblongata arresting the respiratory centre and causing the heart to fail in consequence of the cessation of respiration.

When/

When given to adults, one drachm generally procures from six to eight hours sleep. It is rapid in its action, sleep ensuing as quickly as fifteen minutes or less after its administration. I have never seen any bad effects from its use.

It is a good cardiac stimulant, and does not seem to cause any digestive disturbances or irritation of the gastro-intestinal tract and is superior to Sulphonal in its rapidity of action.

Harmack and Meyer[13] who have investigated its properties, observe that, like alcohol, it first excites and then successively paralizes all the nerve centres, and causes a diminution in the excretion of Urea, and that it cannot be given subcutaneously owing to the pain produced. With regard to the last observation, I do not see that any advantage whatever is to be gained by administering the drug in this manner.

I believe that Amylene Hydrate is specially well suited for mental cases, where sound sleep is quickly desired. In cases of restless Melancholia and Dementia, especially in the old, it seems to have a distinct stimulant action, which gives it an additional value.

In a case of adolescent mania occurring in a boy of sixteen where there was marked incoherence, restlessness/

restlessness, and excitement with delusions, I administered one drachm of the drug at bedtime, the patient getting it daily for some weeks. It invariable caused about six hours' sleep, and no bad effects were at any time observed. After an illness lasting over some six months, the patient quite recovered. In this case the administration of amylene hydrate seemed to have had a very beneficial effect.

There would seem to be some difference of opinion, however, regarding its real therapeutic value. Dr Edwin Dunn[14], who has investigated its action in a number of cases of Epilepsy, concludes by saying: "That it may be useful in mild cases; but it is of no service in severe forms, and possesses no advantages over the bromides." While Bradbury[15] speaking of it as a hypnotic, remarks that "Many undesirable effects have been described, and it would appear even from purely experimental observations, that amylene hydrate is not a desirable hypnotic. And though it has received a fair trial, in mental and other cases, it does not appear to have upheld its reputation. It is, however, comparatively safe and may be used under certain conditions."

On the other hand, Tildermuth[16] has had excellent/

cellent results with it in epilepsy and convulsions. And Whitla[17] says, it has little depressing effect upon the heart, and may be safely given to children. It seldom fails in its action, even in those accustomed to narcotics, and no after ill consequences follow on awaking.

Von Mering asserts that it produces no modification of the circulatory or respiratory organs.

Peiser[18] made investigations regarding the effects of amylene hydrate and chloral hydrate on the excretion of nitrogen in the urine; with the result that he ascertained that, while chloral hydrate increased the nitrogenous waste, amylene hydrate diminished it, and therefore in these cases where there is a large amount of nitrogenous waste and hypnotics have to be continued for long, Amylene Hydrate is to be preferred.

The drug is certainly superior to Chloral, on account of its stimulant action which seems to me to somewhat resemble that of alcohol.

Jennings[19] speaks very highly of amylene hydrate for the cure of morphinomania. In these cases, he has given it in 20 to 30 minim doses by the bowel; and maintains that it is the best drug for such cases. It does not appear to have any cumulative action, and as a rule, the dose does not/

not require to be increased. The sleep is sound and refreshing, and on awakening there is no mental confusion. Headache is rarely complained of. It should be remembered that, like paraldehyde, it is somewhat aphrodisiac in its action, and had better be used with caution in cases of Adolescent Mania with erotic impulse.

The expense of the drug is probably one reason why it has never come very much into prominence; for on the whole it is a safe, reliable and useful hypnotic and one which, I believe, has a future. While at Gartloch I used it extensively and always with the best results.

Amylene Chloral:

A new hypnotic has recently been introduced under the above name. It is a combination of amylene hydrate and chloral, and it is claimed for it that it possesses all the advantages of these two drugs, and may be administered with greater benefit. The drug may be said to be still on its trial and it is as yet premature to express any opinion on it. Those who have tried it speak in favourable terms of its employment.

Group II. The Sulphones

Sulphonal $(CH_3)_2 C(SO_2C_2H_5)_2$

Sulphonal or Dimethyl-methane-diethyl-sulphone is an oxidation product of the union of Ethyl-Mercaptan with Acetone and has, therefore, the composition represented by the above formula.

We owe its discovery to Bauman and Kast. It crystallizes in large colourless tables, and is perfectly devoid of taste and smell. It dissolves in 18 to 20 parts of boiling water and is easily soluble in alcoholic ether or alcohol. It is not affected by acids or alkalies or by oxidising agents generally, either in the cold or warm and is therefore a very stable body.

It is a pure hypnotic and its dose as given in the British Pharmacopoeia is 10 to 30 grains.

Sulphonal is a comparatively new drug, having first come into prominence some twelve years ago.

No one who has worked for any length of time among the insane can fail to have realised the extreme usefulness of this drug. Its tastelessness, the ease with which it is administered, and in the majority of cases its perfect safety, place it at once among the foremost drugs for use in Mental Diseases.

In/

In the violence of acute and chronic mania, and in cases of simple sleeplessness, it is of the utmost value.

I have used sulphonal very extensively in very many forms of mania and sleeplessness, having given it in doses of 15 to 20 grains oft repeated, or in large doses of 40 grains, repeated after a few hours' interval, and have never seen any bad results from its use. It has no effect on the respiratory or circulatory systems.

Sulphonal has no analgesic properties, and always requires a few hours to act efficiently, and in this latter respect it is inferior to Trional.

Whitla[20] speaks of it as having a very slight cumulative action and recommends that it should be given in hot whisky punch on alternate nights. He says, "It is a pure hypnotic, which does not seem to depress the pulse or arterioles or induce a "Sulphonal Habit."

I have always found it best to administer it in milk, or soups, or mixed with tea or coffee. It may be given in combination with other drugs, such as Trional, but I have always used it alone, and found that to be quite satisfactory.

Sulphonal has seemed to me to be most indicated in the restlessness and excitement of chronia mania. Clouston/

Clouston[21] says it is admirable in Folie Circulaire. But in these cases Oswald[22] remarks: "Its administration while lessening the intensity of the excitement has seemed to render the stage of well-being less bright and clear intellectually."

According to Lauder Brunton[23], "Sulphonal from its marked action on the brain cells is one of the best narcotics." In these cases of insanity where patients persistently refuse food it is of great service; because when put under its influence they seem to forget their delusion, and gradually return to the habit of taking their food naturally. Clouston[24] even refers to sulphonal as having curative properties.

On the other hand Oswald[25] and more recently, Hotchkis[26], have each related a case of the peculiar condition, known as Haematoporphyrinuria, in which the substance Haematoporphyrin is excreted in the urine, as the result of the administration of Sulphonal. Both cases terminated fatally. In the former's case the patient had in all 2200 grains of Sulphonal in about 90 days. In other reported cases 8000 grains were given in 120 days, 800 grains in 40 days, and 400 grains in 25 days; and Oswald[25] remarks: "It seems probable that an explanation of the fatal issue in many of these cases, may be found in a cumulative action of the sulphonal affecting the/

the adrenals leading to a rapid destruction of blood and to such an accumulation of the decomposition products of Haemoglobin, as to give rise to serious effects on the nervous system, and to death."

In the latter case, the peculiar coloration of the urine - which is of a deep claret shade - had ceased a week or more before death; and Hotchkis concludes by saying: "Surely, then, the great lesson to be learned from such cases is never to give sulphonal for any length of time, if indeed, at all, unless one is certain that the kidneys are healthy."

This peculiar condition of Haematoporphyrinuria is now well recognised, between forty and fifty cases having, by this time,been reported; of these about one half have died; and it is interesting to observe that in nine-tenths of the cases, the patients have been women.

Wien(27) only recently cites another case of poisoning with sulphonal, and it would seem that in all these cases there is a striking similiarity in the symptoms. For this reason, it seems clear that the drug is contra-indicated in all cases where there is suspected kidney mischief.

In any case the patient should always be carefully watched, and the urine carefully examined from time to time. If toxic symptoms should appear, the only treatment of any avail is the free exhibition

exhibition of alkalies.[28]

When taken for any length of time, it sometimes causes the patient to experience a tottering sensation when walking, or standing, as if he was going to fall; sometimes a comparatively small dose will cause this.

Kisch[29] relates a case of a man aged 62 with senile insomnia in which 15 grains had a good effect, but he felt drowsy all the next day, and was unable to stand up.

Whitla[30] observes that "ataxia with staggering gait occasionally follows the use of the drug and after full doses the inco-ordination has appeared to resemble drunkenness."

In a few cases, that I have observed myself, when large doses had been given, it seemed to me that some of the patients in walking or standing erect had an inclination "to give at the knees."

William J. Smith[31] in an article on the chemico-physiology of sulphonal, in which he has studied,

I. The action of the drug on the activity of the tissue changes; and
II. The changes in the sulphonal during its passage through the organism,

summarises his results thus:--

I. Sulphonal in moderate doses is completely changed during its passage through the body into a sulphuretted/

sulphuretted organic substance, such change being the more remarkable because sulphonal is extremely stable, and because some allied bodies viz.,

Ethylenediethylsulphon

$$\begin{array}{l} CH_2 - SO_2 - C_2H_5 \\ | \\ CH_2 - SO_2 - C_2H_5 \end{array}$$

pass into the urine unaltered.

II. The elimination of sulphuric acid is not increased by taking sulphonal, showing that the substance formed from it must possess considerable stability.

III. Sulphonal in moderate doses does not affect the metabolism of the nitrogenous tissues, and A. Cramer[32] has shown that it does not disturb the function of the stomach and bowels.

In an article by Dr H. Rosin[33] he concludes thus: "On the whole, sulphonal in doses of two grammes (half a drachm) is as certain in its effect as morphine or chloral, and in cases of simple insomnia may be recommended in doses of double that strength on account of its freedom from after effects."

I think that there can be little doubt that, the exact mode of action of sulphonal is not yet clearly established. Vanderlinden[34] and De Buck put forward the view that the hypnotic action was due to a diminution in the alkinity of the blood, and a resulting accumulation of CO_2 combined with poverty of O in the nerve cells; but this view - ingenious as it is - has been controverted by several other observers.

Its hypnotic action seems to be that of causing

a/

a temporary paralysis of the brain cells; and it now seems to be quite certain that it also acts on motor nerves, so as to cause a temporary paralysis of their peripheral endings.

(55) The urine of patients taking sulphonal is stated to reduce Fehling's solution.

To sum up, the following points should be attended to in its administration:--

1. The patient should get the drug an hour before bedtime, when it may be given in a hot drink. If it is taken cold it takes longer to act, and requires to be given three or four hours before retiring to rest, when it may be administered in the form of cachets, capsules, compressed tablets, or in powders, spread between thin slices of bread and butter.

2. The urine should be examined from time to time.

3. It should not be administered where there is any kidney weakness.

4. The bowels should be kept open.

5. The patient must be kept warm and as much as possible in an equable temperature.

6. The drug if given for a long period should be stopped occasionally for four or five days at a time.

7. Its use should at once be discontinued on the appearance of any paralytic symptoms.

8. Small doses oft repeated - as in violent mania, etc., - are to be preferred to large ones.

9. If administered in any quantity and for a long period, the patient should be observed daily.

I would add that sulphonal seems to me to be one

of/

of the best hypnotics. Firstly, in that it best imitates Nature's sleep, and when the patient awakes he nearly always feels refreshed and not as if he had had a "drugged sleep."

Secondly, in the vast majority of cases it is perfectly safe and there is a complete absence of after bad effects.

Trional:

This substance, which is allied to sulphonal, differs from it chemically in possessing an additional ethyl group, being:

Di-ethyl-sulpho-methyl-ethyl-methane,

while sulphonal is:

Di-ethyl-sulpho-dimethyl-methane.

It exists as a white crystalline powder with a faintly bitter taste, is slightly soluble in water, is soluble in alcohol and in ether. Compared with sulphonal and tetronal it is the most soluble. Dose, 10 to 30 grains.

This drug is very similar in its action to sulphonal, but it is less cumulative and acts more quickly, generally producing a longer sleep. It acts on the cortex of the brain.

Trional has no analgesic properties and is practically free from smell and taste. I have not used/

used it nearly so frequently as the foregoing; but in these cases where hypnotics are being continued for any length of time, viz. in the case of the long continued use of sulphonal, it is sometimes useful to intermit with trional for a short period.

It seems to be a very safe drug. On the other hand, if given for any length of time, Haematoporphyrinuria may be induced, just as in the case of sulphonal. It does not seem to have been given nearly so much as sulphonal, probably owing to the fact that it costs more and is not so easily administered. It is somewhat constipating in its effects but is much safer than chloral. Goldmann(36) "finds that trional is preferable to sulphonal. Its action is much more rapid and certain. It does not accumulate in the system as does sulphonal and it does not irritate the kidneys and intestines in its elimination. Full doses of it are not so apt to produce Haematoporphyrinuria as are full doses of sulphonal."

As regards the administration of trional it may be given stirred up in milk or taken in cachets. The latter is probably the best method, though not always suitable in mental cases. It is fairly rapid in its action, sleep generally ensuing very shortly after its administration. Whitla(37) has noticed/

noticed that when given in some cases of fever, it has upset the digestion. He speaks of it as being probably "the safest of all the newer hypnotics."

It is not so suitable for alcholic insomnia as chloral; and in large doses it may interfere with the power of co-ordination, just as in the case of sulphonal.

In some cases, where Sulphonal has failed, trional has proved effectual. Dr A. Claus of Ghent[38] who has made investigations on its use, finds that "It is especially valuable in the nightmares or night terrors to which nervous children are so subject, and also when the sleeplessness is associated with chorea or convulsions. It does not disturb the mental, circulatory or respiratory functions and acts rather beneficially than otherwise on the digestion." The doses recommended by Dr Claus are as follows:

Children less than twelve months,	3 to 6 grs.
One to two years,	6 to 12 "
Two to six years,	12 to 18 "
While up to ten years he gives	18 to 23 "

Bauman and Kast[39] carried out a series of experiments on dogs with sulphonal, trional, and tetronal, and concluded that their hypnotic action increased with the number of ethyl groups in their molecules. And since sulphonal contained two ethyl groups/

groups, trional - three, and tetronal - four, they came to the conclusion that tetronal was the most potent hypnotic of the three. At first sight, this seems to be a very feasible theory, but further research however has shown that it is not so.

With regard to the toxic effect of trional: a case is related by Collatz[40] where a young man, who suffered from epileptic fits, attempted to commit suicide by swallowing 120 grains of the drug. In about a quarter of an hour he had an epileptic fit, which lasted about five minutes; he then complained of nausea, but did not vomit; he then went to sleep and slept 12 hours, his pulse and respiration being normal. The next day he slept a great deal and in the evening complained of abdominal pain and retention of urine, for which a catheter had to be passed and 400 cc. drawn off. This was of a dark colour and free from albumen, sugar and haematin. On the succeeding day the man was quite well.

M. Vogt[41] observes that "Toxic urinary symptoms are only manifested when the urine is strongly acid in reaction. The symptoms are oliguria and haematoporphyrinuria." And further he recommends that bicarbonate of soda be given during the day to patients taking trional, so as to reduce the acidity of the urine.

I/

I think that this latter observation is of considerable importance, as it coincides with the recommendation of the Clinical Research[42] workers, who say that the free exhibition of alkalies is the only treatment of any avail in cases of poisoning by sulphonal or trional.

Lastly, I would add that trional seems to me to be a perfectly safe hypnotic in the vast majority of cases; but that its use should not be continued for any length of time; and when given, all these precautions should be attended to, which were indicated when treating of the administration of sulphonal.

Tetronal:

This drug is analogous in composition to sulphonal, but with the two methyl groups replaced by ethyl. It is Diethylsulphon-diethylmethane. It occurs as a white crystalline odourless powder. Dose, 15 to 30 grains.

This substance resembles sulphonal and trional in its general effects. I have never employed it myself and am therefore unable to speak of its uses from personal observation.

Whitla[43] observes that "Its indications are the same as those for sulphonal, but in some very obstinate/

obstinate nervous conditions it has given better results, though it often failed in conditions like Delirium Tremens."

Drs Raimondi and Mariottini, who have made a very exhaustive investigation into the actions of trional and tetronal, conclude that of the two, the former is to be preferred.

Tetronal, though not by any means an unknown drug, is one which does not seem to have come much into prominence and appears to be but little used. The literature on the subject is scanty. Like trional its hypnotic action is on the cortex of the brain, sleep coming on soon after its administration, not some hours afterwards, as is generally the case with Sulphonal. But, I do not think that it has anything to recommend it in preference to these two hypnotics, which have just been considered.

Before finishing this account of the Sulphones, I would add that in mental disease at least, sulphonal when judiciously administered is mostly to be preferred to trional.

Group III. Chloral and Allied Substances:

Chloral Hydrate $CCl_3 CH(OH)_2$

Chloral Hydrate or Trichlorethylidene Glycol, is/

is obtained by the addition of water to the liquid chloral produced by the action of dry chlorine gas on ethylic alcohol.

Solubility, 4 in 1 of water, 5 in 1 of alcohol (90%) 2 in 1 of Glycerine. Dose 5 to 20 grains. Occurs in colourless monoclinic plates, which do not deliquesce on exposure to the air. It has a pungent but not an acrid odour and a pungent and rather bitter taste.

There is one preparation of this substance which is official, namely Syrup of Chloral, of the strength of 10 grs. to the fluid drachm. Dose, ½ to 2 fluid drachms.

Chloral Hydrate was first discovered and introduced into medicine by Liebreich and Dumas about the year 1869. And since then it has become a universal remedy in insomnia, and one that is deservedly popular, though it is not without its dangers.

Its action as a hypnotic differs at once in very many respects from these drugs which have just been considered.

In Chloral Hydrate we have a powerful hypnotic which is depressing, and one which when pushed to excess, exerts a very depressant action on the heart.

In speaking of this drug, it is regrettable that/

that in the hurry and work of hospital and asylum practice, I did not find time to keep a written record of its effects in the cases in which I administered it. But having now dispensed and given chloral on very very many occasions, for all forms of excitement and insomnia in mental disease, and at a later date, in infirmary practice, I feel that I am able to speak with considerable confidence regarding its effects.

In simple insomnia caused by nervous worry or mental excitement, Chloral administered in 10 to 15 grain doses, is a most satisfactory hypnotic. In such cases, more especially in old people where there is a lowered condition of the vitality, and general nutrition - a state of matters which of itself tends to insomnia - I have frequently given chloral made up as in the following prescription:

R.

Syrup Chloral	℥ i.
Spt. Ammon. Aromat.	℥ i.
Whisky	℥ fs.
Aquae ad.	℥ q.s.

M.

Sig. The draught to be taken at bed-time.

In this combination the addition of the Sal: Volatile and whisky quite counteract any depressing effects which the chloral may exert, and the result is that a refreshing sleep is obtained, which generally/

generally lasts throughout the whole night. In mental disease and I would say in all forms of such disorder, Chloral should not be given for any length of time, or in any great quantity; for it seems, although causing sleep, not to possess any curative properties, and to be generally depressing in its effects. Indeed, it is questionable if the effect of chloral long continued is not directly prejudicial to the cerebral tissue. The majority of the authorities on the subject seem to be agreed that it is. Clouston[44], speaking of Chloral, says: "My experience is that it has a subtle influence for harm on the brain when much given, by which the organ loses that quality which we call tone. The patients cannot bear pain so well. They have not the resistive power, and they are apt to look pale and unrefreshed in the morning," and Sherlock[45] remarks: "It is not considered to be a remedy having much curative power over the progress and course of mental disease, but it is of undoubtedly high value in procuring rest and sleep, without much, if any, constitutional disturbance; so that time is afforded for the due exercise of other moral and medical treatment."

In Chronic Mania where there is constant restlessness and excitement, worse at night, Chloral is of great value. In these cases it is always best/

best given combined with the bromides, say, 15 to 20 grains of chloral along with 30 to 45 grains of potassium bromide. Such a combination, when given at bed-time will frequently cause six to eight hours sleep.

In Acute Mania, especially when it is caused by alcoholism as in Delirium Tremens, chloral must be used with caution, for in these cases there is often a tendency to heart failure, as I have before observed, and where such is suspected it is perhaps better to withhold chloral altogether or only give in small doses, watching its effects very carefully.

Clouston[46] recommends chloral combined with the bromides in 15 or 20 grain doses for short periods, especially in Alcoholism. But he adds that he does not consider it such a valuable drug now as he used to do formerly, saying that it tends towards thinness and a haggard look.

Whitla[47] remarks that after the delirium has lasted several days chloral is a dangerous remedy, which must be used with great caution, if employed at all, as the heart at this time is especially susceptible to its action. He believes that the use of chloral as a hypnotic in this disease actually raises the mortality and accordingly, he has ceased to use it in this connection.

In/

In the majority of cases of acute mania in which I have administered chloral, it has proved a valuable sedative - if not too long continued. But it must be admitted that, in a few cases, its effects have been disappointing.

In Epilepsy, where there is violence and mania, chloral is of great service combined with bromide of potash. In these cases, I used frequently to give 15 grains of chloral three times a day combined with double the quantity of potassium bromide. Also, in the sleeplessness of Melancholia, small doses of chloral at bed-time, such as 10 or 15 grains with the bromide of potash and a little whisky are very effective, sleep generally ensuing within about 30 minutes.

Saunders says:(48) "Patients who have passed sleepless nights in spite of the ordinary treatment by morphia, henbane, etc., have, after a two scruple or drachm dose of the chloral hydrate, passed a tranquil night and had undisturbed rest, lasting from six to twelve hours."

In some cases the "Chloral Habit" has been induced. Clouston(49) relates that he has seen two cases of insanity brought on by its constant use. But this is comparatively rare. In ordinary cases, there are no bad effects to be observed from its careful/

careful employment. The appetite is not impaired, nor are the secretions in any way affected. Physiologically it seems to act directly on the cerebral hemispheres, producing sleep. The pulse is not much affected. It causes a dilatation of the arterioles, and slight dilatation of the pupils. Respirations are full, deep and regular. When a large amount is given, the sleep becomes deeper, the respirations fall in number, the pulse is weakened, the temperature reduced. There is relaxation of the whole muscular system. Sensibility and reflex action are diminished, and the patient may pass into coma, and finally death occurs by the toxic action producing cardiac syncope.

It is to be noted that in the milder degrees of sleep, there is no anaesthesia. The physiological action of chloral is well summed up by Wood(50) who says: "Upon the cerebrum it acts as a very powerful and certain hypnotic; in full doses it acts as an intense depressant upon the centres at the base of the brain, and upon the spinal cord, and also causes slowing and weakness of the heart's action, probably vaso-motor paralysis, slowing of the respiration, and muscular weakness with a certain amount of anaesthesia; in fatal doses it usually produces a gradual death by paralizing the nerve centres/

centres in the medulla and thereby arresting respiration, although in rare cases it kills suddenly by directly paralizing the heart, which always stops in diastole. Its action in very small doses is uncertain, but there is considerable evidence to indicate that it irritates or stimulates the spinal and the cardiac and even the vaso-motor centres. On the vagi and on the motor nerve trunks it has no marked influence."

Chloral does not affect the bowels: but if continued for long a rash - affecting the face, arms, and neck, may be induced - but this is rare. I have not observed it myself, and it would seem in these cases in which its presence has been recorded to have been produced more by idiosyncrasy than otherwise.

It is asserted that the long continued use of chloral will produce sickness and vomiting; but this also, I have never observed.

On the whole, I have always found it best, not to administer chloral alone, but combined with other drugs, as I have before indicated. There is, however, one exception to this: I refer to its use in "Congestive Attacks", so common in all large asylums. In these cases I have always used chloral alone, giving it in 20 grain doses, by the mouth if the patient could swallow, and failing that, by the rectum/

rectum. In such cases its use is of the greatest value. Its action markedly lessens the severity of the attacks, and in some cases may stop them altogether.

Some suggest giving opium along with chloral; but I would point out that this seems to be a very dangerous combination, and one that should only be employed with the utmost caution; if indeed at all. I have never given it myself, but I have heard of dangerous effects from its use when in the hands of others. In cases of very acute and violent mania, chloral may - on an occasion - be administered during the day; but in the vast majority of cases, its use had better be put off until bedtime, and then it may be given.

Clouston[51] tells of two patients who died suddenly during a sudden burst of mania; each at the time were under the influence of moderate doses of 30 grains. On post-mortem examination, the blood was dark and fluid; the right side of the heart and lungs engorged, as of a sudden paralysis of the breathing centre in the Pons. Since then he has never given chloral as a sedative during the day, but always at night or after or during convulsions, and then always in small doses of 10 to 25 grains along with from 30 to 60 grains of bromide of potash. But in/

in such cases, he prefers paraldehyde.

Chloral is not cumulative in its action, indeed its effects too soon wear off, and the dose has to be increased.

It is much inferior to opium, in so far as it possesses no analgesic action, for such effect as it possesses in this respect is practically nil when used in small doses. But on the other hand, it does not set up the gastric disorder and constipation so often caused by that drug.

As regards its effects when compared with sulphonal, I think that the latter drug is distinctly to be preferred, at least in these cases where the use of hypnotics is likely to be long continued.

I doubt if the sleep produced by chloral is really very refreshing. One is naturally always sceptical with regard to the invigorating effects of sleep induced by the use of drugs, and that produced by chloral, though sound at the time, is I fear, rather of the nature of a "drugged" sleep.

It has appeared to me from my own experience, that chloral generally acts better in Acute Mania - not caused by alcohol - than in the ordinary cases of Delirium Tremens.

In Asthma, where the insomnia is frequently so peculiarly distressing, I have given chloral with the/

the very best results. Indeed, I have seldom seen a case of asthma which was not to a great extent relieved by its administration, along with some Sal Volatile and a little stimulant, such as brandy or whisky. In heart disease and where the heart is fatty, chloral is contra-indicated.

Sleep is generally produced in about 20 minutes to half an hour, after a dose of it, and on awaking there seldom seems to be any confusion of intellect or headache, etc.

It has a powerful influence in lowering the bodily temperature, and it is important when using it that the patient be kept warm and well covered up in bed, lest a chill be induced.

Whitla[52] observes that the temperature falls from $\frac{1}{2}$ to $1\frac{1}{2}^{\circ}$ Fahrenheit, after ordinary hypnotic doses. That the drug appears in the urine, and if this secretion be alkaline, it may change the Chloral into Chloroform.

Lauder-Brunton[53] found that the fall of temperature was so great, as to alone cause death.

It is sometimes very remarkable how one single dose will sometimes greatly benefit a patient. Dr Saunders[54] of Devon Asylum, who was the first person in this country to employ chloral in the treatment of the insane, relates a case of a man suffering/

suffering from recurrent suicidal melancholia with excitement, who suddenly became noisy, and in an excited tone carried on an imaginary conversation with the Devil, who was tempting him to dash his brains out and upbraided him for his cowardice in not at once doing so. A drachm dose of chloral was prescribed, and in twenty minutes, he fell into a sound sleep, from which he awoke much refreshed both in mind and body. On the second day after the attack, he was pursuing his employment in his usual state of health. He had had several previous attacks, which had yielded to treatment by other remedies; but the prompt action of the drug in this instance was very marked.

When chloral first came into use Liebreich, its discoverer, believed that it acted by being split up into Chloroform within the system; but more recent researches have shewn that this was an entirely erroneous idea, though at first sight it would seem to have been feasible enough.

Sleep is caused by the direct action of the drug upon the cerebrum. Lauder-Brunton(55) expresses this very clearly when he says: "In the first stage of excitement, the circulation in the brain is somewhat increased, but as sleep comes on the vessels contract and the brain becomes anaemic."

The/

The soporific effects of chloral on the cerebrum are particularly well seen in its sedative action in the insomnia following convulsions, and that caused by the later stages of Bright's Disease.

Chloral must always be administered well diluted; otherwise, it is apt to set up gastro-intestinal disturbance and its action becomes delayed.

In the insomnia of cardiac asthma I have found the following combination to be most efficacious, when taken last thing at night.

R.

Chloral Hydrate	grs. xv
Potass. Bromid.	grs. xxx.
Spt. Chloroform	℥ i.
Aquae ad:	℥ ii.

M.

Sig. The Draught to be taken at bed-time.

Lastly, it is much to be regretted that chloral - on account of its cheapness - is so easily procured by all classes of the community, by whom it is not infrequently put to criminal uses.

As I am writing, a case is reported as having recently occurred in Glasgow, where a man was successfully 'drugged" - for purposes of robbery - by having had ten grains of chloral administered to him in his beer. And in the expert evidence given at the trial by Sir Henry Littlejohn, he is said/

said to have severely animadverted on the facilities which at present exist, for obtaining such a potent drug. As is well known, chloral when given in beer or porter has a peculiarly soporific effect.

Butyl-Chloral Hydras: $CH_3\ CHCl.\ CCl_3\ CH(OH)_2$

Butyl-Chloral Hydrate or Trichlorbutylidene Glycol. is obtained as follows:- Dry chlorine gas is passed through Aldehyde Butyl-Chloral is formed. This is separated by fractional distillation and water added.

Characters: Pearly white crystalline scales with a nauseous taste and a pungent odour resembling chloral hydrate. Solubility, 1 in 50 of water, freely in spirit and glycerine.

Dose 5 to 20 grains.

Butyl-Chloral Hydrate is sometimes designated by the name of Croton Chloral Hydrate, but this term is incorrect and should be abandoned.

We are indebted to Dr Oscar Leibreich for having introduced this substance into medicine. It somewhat resembles chloral hydrate in its action, only on the whole it is a weaker and less certain hypnotic and is not so depressing in its effects. The drug is perhaps of most use from the fact that it appears to have a specific action on the fifth nerve/

nerve and on that account is most beneficial in conditions of Neuralgia, such as Tic Douloureux; in this affection it seems to have a marked analgesic action. Liebreich[56] affirms that anaesthesia first begins in the head, then follows narcosis; but anaesthesia in the head and face may be complete before any narcosis manifests itself. Owing to this fact he suggests its use in operations on the face and in vivisectional experiments; because unlike chloral, its toxic effects, first affect the respiration, the heart being only affected secondarily. He recommends that it be administered dissolved in glycerine and water rather than in alcohol in doses of 15 to 30 grains.

There would seem to be some difference of opinion however, with regard to Liebreich's observations, for Wood[57] says that the researches of Mering and Lahousse have not borne out his (Liebreich's) assertions; and that its action would appear to be completely parallel to that of chloral.

Observers in this country also seem to differ widely regarding its real therapeutic effects, for Whitla[58] describes it as possessing properties similar to chloral hydrate, from which, however, it differs in being a weaker hypnotic and in producing somewhat less cardiac depression; while Bradbury[59] holds/

holds that it is more toxic, more hypnotic and more depressant to the circulation.

On the whole the weight of evidence seems to point to the fact that butyl-chloral Hydrate is not very effective as an hypnotic; and in these cases in which it is given, it is more on account of its analgesic effects in cases of Neuralgia of the fifth nerve. In this connection Riddell[60] speaks very highly of it. He combines it with digitalis and recommends that it should be administered in solution and in much larger doses than those allowed by the Pharmacopoeia.

Wood[61] says, the safest plan is to give 5 grains every half hour, until 30 grains have been taken, or relief afforded.

Ringer[62] has found it very useful in Migraine, and in Neuralgia of the back of the head, and also that of the neck, with pain radiating to the shoulders; but says that there is little evidence at present as to its effects on neuralgia of the other parts of the body. He considers the drug a valuable one in these affections, and is of the opinion that Liebreich greatly underrates its efficacy.

Dr Yeo recommends it in the "distressing night cough of phthisis." In asylum practice, butyl-chloral hydrate has not taken a high place amongst hypnotics/

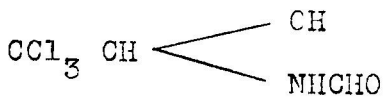
hypnotics, and it would seem to be of most value on account of its peculiar analgesic action.

As regards its administration, Lauder Brunton (63) recommends that it should be given in syrup of Tolu or suspended in almond mixture or mucilage.

If administered in pill form, the pills should be made fresh.

Chloralamide:

Chloral Formamide or Chloralamide is a synthetical product derived from chloral anhydride CCl_3 CHO and formamide CHO OH_2 and has the formula:



This substance was first introduced into medicine by Von Mering and occurs in colourless crystals, which are slightly bitter to the taste.

Solubility - 1 in 21 of water, 1 in 2 of alcohol (90 p.c.)

Dose 20 to 45 grains (Not official) -

Chloralamide is of comparatively recent introduction. During the time it has been before the Profession, it has been very extensively tried, and there are many reports of its therapeutic actions which speak in favourable terms of its use. Generally speaking, the drug is supposed to have the properties of chloral hydrate without the depressing/

pressing effects of that substance.
It should never be prescribed with alkalies, for their action is to decompose it, nor should it be given with hot water, for the same reason.

On the very few occasions on which I have administered this drug, I gave it while the patient was having sulphonal, so that possibly the soporific effects which I obtained were in part due to the latter hypnotic. Its results in the hands of others however, seem to have been on the whole very satisfactory.

I am inclined to think that in very intractable cases of insomnia - as sometimes occurring in chronic mental disease - chloralamide given alone may not prove to be of much use; but in cases where other hypnotics are being administered for a long period, it may sometimes be found beneficial to intermit their administration for a short time by its employment. All observers seem to be agreed as to the safety of chloralamide, indeed very few ill effects appear to have been observed. Occasionally headache has been complained of.

Paterson[64] after having given it an extensive trial, concludes by saying:

"That this drug will be a valuable addition to our therapeutical armamentarium is undoubted.
So/

So far as can be judged from the published reports, we are justified in considering that as an hypnotic it has proved itself efficient, but whether equal to Chloral remains as yet doubtful; while its freedom from injurious action and the safety with which it can be administered give it a claim which merits our highest consideration."

Chloralamide is said to possess slight analgesic properties, and its hypnotic power has been roughly estimated as about two thirds that of chloral. It is claimed for it that the dose does not need to be increased and that it tends to establish a "sleeping habit."

Whitla[65] says that it is safe, but less certain than chloral, that there is no dilatation of the arterioles or fall of blood-pressure, and as yet, no depressant influence on the heart and respiration has been noticed.

I think it should be mentioned, as worthy of our observation, that a skin eruption has been noted as following its exhibition. Pye-Smith[66] relates the following case of Universal Dermatitis which was apparently due to the administration of chloralamide. The patient, a man aged forty, suffering from aneurism, was prescribed among other hypnotics, Chloralamide in full doses, and with apparently good effect/

effect. Soon after, acute inflammation appeared on the face, with Coryza. Stomatitis, and raised temperature This rapidly spread over the whole body, the urine was febrile and slightly albuminous, and pyrexia continued for a week. Profuse desquamation followed, resembling that of Exfoliative Dermatitis, and the skin finally resumed its normal appearance.

In this case the patient had received 80 grains altogether, given in two doses of 40 grains each, one dose having been administered at 8 o'clock in the evening, the other at 4 in the morning.

Skin eruptions following the use of chloralamide, are, however, decidedly rare and when they do occur are more probably due to some idiosyncrasy on the part of the patient than otherwise.

Bevan Lewis[67] reports having found the drug to be most useful in the insomnia of Melancholia, Alcoholic Paralysis and General Paralysis of the Insane. He asserts that it retards the digestion of fibrin. This last fact appears to me to greatly militate against its employment, for I am strongly of the opinion that any gastric disturbance, however mild, arising from delayed digestion, is a most important factor in the causation of insomnia. whether it be in the sane or insane.

(The/

(The reader may remember that when speaking of paraldehyde, I emphasised the fact that it had been shewn to be of value in assisting in the digestion of fibrin - a matter of no small importance.)

Wood and Cerna[68] who have investigated its action on animals, are of the opinion that it induces sleep by acting on the cerebral cortex, and that it is a feeble spinal depressant.

They say that it has a powerful influence on the respiration, in moderate doses, increasing its rate and also the amount of air breathed; in toxic doses, however, death is produced by paralysis of respiration.

From Wood's own experience, the drug seems to be slower and somewhat less sure in its action than chloral, rarely producing unpleasant after-effects.

Strahan[69] who has given it over 200 times in cases of insanity, sums up its effects as follows:-

1. Chloralamide is a very effectual hypnotic.
2. It appears to have no depressing effect whatever on the heart.
3. The dose is about 35 to 45 grains, but 55 grains may be given with safety.
4. It should be administered an hour, or an hour and a half, before the time sleep is desired.
5. Its action is in some cases deferred so long as three hours, even in cases where it gains prolonged sleep.

6/

6. No ataxic symptoms or headache follow its use.

7. It does not affect the digestive system.

8. It is a very useful and safe hypnotic, and may be given to paralytics whatever their stage.

9. In my opinion, it is equal, but in no way superior to paraldehyde, save that it is much pleasanter to take and does not impart to the breath any such disagreeable odour as does the latter drug.

Some have recommended its use in cases where, on account of cardiac disease, Chloral is contra-indicated, and it has been given in insomnia with "irregular" heart after influenza.

It may be mentioned here that Chloralamide is half the price of Sulphonal.

I would now briefly consider two other drugs, which in some respects are somewhat similar to it, namely:- Chloralimide and Chlorobrom.

Chloralimide was brought in by M. Choay(70) in collaboration with M. Behal. Its formula being CCl_3 CHNH. It is prepared by the action of heat upon Chloral Ammonium and crystallizes in long needles, being colourless, odourless and tasteless. It is insoluble in water, but soluble in Alcohol, Ether and Chloroform. Dose 5 to 20 grains.

This drug when it first came in was said to be superior to Chloral and Chloralamide. Choay(70) stated/

stated that in doses of 5 to 8 grains, it was analgesic, and antipyretic to a remarkable degree.

Now it is seldom heard of and the literature concerning it is scanty; altogether it does not seem to have upheld its reputation, and Whitla[71] remarks that it will soon be forgotten.

Chlorobrom: This is a preparation containing 30 grains of Chloralamide and 30 grains of Potassium Bromide in each ounce; flavoured with Tincture of Orange and Chloroform Water. Dose ½ to 1 fluid oz.

This preparation was brought in some few years ago by the late Professor Charteris of Glasgow University. He held that it was of great value, not only as an hypnotic, but also in sea-sickness. In an account which he has given of it, he says: "The habit of taking the solution does not grow on the patient and its exhibition is attended by no depression or derangements of digestion."[72]

We do not seem to hear so much about Chlorobrom now-a-days, and I think that it is a pity. I used to administer the preparation frequently as made up in the following prescription.

℞.

Chloralamide		
Potass: Bromid:	ana	℥iv.
Spt. Chloroform		℥ii. fs.
Aquae ad:		℥viii.

M.

Sig. Two tablespoonfuls for a dose at bedtime.

And it almost invariable gave good results. It is a comparatively safe hypnotic and may quite well be given in doses up to 6 drachms. I have never seen any bad effects from its use.

Lothian[73] who employed it in Delirium Tremens says: "I think this solution is not widely enough known in the profession; but I feel certain that in cases of insomnia and Delirium Tremens as an hypnotic agent, it stands pre-eminent."

Charteris has given a most interesting account of its virtues in sea-sickness in the Lancet for 1894, Vol.I. p.1001.

Chloralose: Anhydro-Gluco-Chloral, occurs as a white crystalline powder, melting at 187°C. soluble in Alcohol, but only slightly so in Water or Ether. Dose 3 to 10 grains.

This is a new hypnotic, introduced a few years ago by Hanriot and Richet, and obtained by the action of Chloral on Glucose.

Reports on its action are somewhat conflicting. When first brought in, its discoverers held that it was superior to Chloral in its general effects; but this seems far from being the case. When administered deep sleep quickly ensues, sometimes accompanied at its commencement by some degree of excitement/

excitement with tremors and twitchings of the limbs, and in some cases, incoherent speech, slowness of pulse, involuntary passage of urine and faeces, along with coldness of the skin and dilatation of the pupils have been noted. Certainly most undesirable effects. However, it is only fair to state that in the hands of some observers, Chloralose appears to have afforded satisfactory results.

Leon L'Hoest[74] affirms that he administered it to Melancholics and Neurasthenics with good results, and in cases of excitement, its exhibition was absolutely favourable; sleep generally lasted from 6 to 8 hours and was peaceful without dreams, the patients waking easily without heaviness or headache. He sometimes gave it in solid food, but recommends a simple infusion to facilitate its assimilation.

Marandon de Montyel[75] found it useful in cases of Epilepsy complicated with insomnia, as it appeared to produce sleep, and cut short the period of excitability.

On the other hand, Lombroso[76] denies that Chloralose is entirely harmless; he has seen the occurrence of tremor, followed by complete loss of memory after its administration. In another case intense prurigo was caused, while in a third, there were symptoms of paresis with threatening asphyxia.

Ohmjelewski/

Ohmjelewski[77] tried it in 17 cases of mental disease, and in three of these, transient tremor of the upper limbs was observed before the patient fell asleep. In five considerable perspiration occurred, and in two considerable excitement followed its administration.

Two cases of poisoning by Chloralose are described by Touvenaint[78] in which the symptoms were, malaise, general tremor, incoherent speech, inability to move, nausea, difficulty of swallowing liquids, and deafness; followed by dilatation of the pupils, coldness of the skin, slow pulse, torpor, and involuntary passage of urine and faeces, etc. Already many untoward effects have been recorded from the exhibition of this drug; and observers in this country do not seem enthusiastic in its support.

Personally, I have no experience of Chloralose myself, but from a study of the various accounts of its therapeutic actions which have appeared from time to time, I should be very chary about using it.

It does not disorder digestion and is said to be best administered in cachets, as it is both bitter and insoluble.

Chloral Urethane ($C_5H_8NCl_3O_3$)

This substance which is also known by the name of/

of Ural or Uralin, was brought in comparatively recently by Poppi. It is prepared by mixing a solution of Chloral and Urethane with strong Hydrochloric acid, and is obtained as a white scaly mass, almost insoluble in water, but easily soluble in Alcohol and Ether.

Poppi claimed for it that it possessed all the advantages of Chloral, without its depressing effects, which were counteracted by the Urethane. The drug, however, does not seem to have found general favour, and there is not much heard about it now. On the whole, it is a safer, though a less certain hypnotic than Chloral.

C H A P T E R III.

HYPNOTICS (continued)

Group IV. The Bromides and Cannabis Indica.

The Bromides: These comprise a group of salts which are mainly sedative and hypnotic in their action.

Bromide of Potash: Occurs in colourless cubical crystals, with no odour, but with a pungent saline taste. Soluble in 2 parts of cold water and in 200 parts of alcohol (90 p.c.)

Dose 5 to 30 grains.

I describe this substance, as it is one of the most important of the bromide salts, and one whose therapeutic actions may be considered as typical of all the others.

When administered internally, it acts as a powerful sedative and hypnotic, being quickly taken up by the blood and circulated through the body, causing a general sedative effect, accompanied if the dose be large enough, by drowsiness and languor. This it does, by diminishing the quantity of blood in the cerebrum, and lessening the reflex excitability in the cord, and cortical motor centres.

It is excreted as Bromide of Soda by the skin, breath/

breath, kidneys and faeces, appearing very soon in the urine. In those who have taken it for some time and are fully under its influence, there is always some degree of anaesthesia produced at the back of the pharynx. This can easily be demonstrated by sweeping round the finger just beneath the soft palate, and if the patient be fully under its influence, there will be an absence of all reflex spasm and retching.

The general sedative, and to a lesser degree hypnotic effects, which are produced in those taking the bromide salts, renders their administration of the utmost value in cases of sleeplessness and general restlessness, the more especially in those subjects where the insomnia is brought about by overwork and worry.

Indeed, Bartholow[1] says: "No clinical fact is more conspicuous than that the Bromide of Potassium will relieve wakefulness of this kind."

It must not be supposed, however, that the administration of the Bromides is applicable to everyone of these conditions, for this is far from being the case.

In all anaemic conditions, they are contra-indicated, and indeed in these cases where their administration has been continued for any length of time/

time, anaemia is apt to be produced in greater or less degree.

I do not think that they are of very much service when given alone, except in cases of Epilepsy, of which I will speak anon - and in some of the lesser degrees of insomnia, where they may be prescribed with considerable advantage, as in a 40 grain dose, repeated within one or two hours if necessary, just to - as it were - break the "habit of sleeplessness."

If they are to be relied upon entirely to produce an hypnotic effect, very large doses must be employed, and I do not think that there are many cases in which this is desirable. Still, in some of the severer forms of mental disease, when given alone and in large quantity, they are sometimes of decided benefit. In this connection, I would just briefly mention a somewhat exceptional case of the kind, which came under my observation a short time ago. The patient was a married woman, of about 40 years of age; she had had a large family and had had some three or four previous attacks of insanity. At the time I saw her, she was suffering from a severe exacerbation of chronic mania, in which she was very noisy, violent and generally unmanageable. For this attack she had received 22 drachms (nearly 3 oz.) of Bromide of Soda in the 24 hours, given in varying/

varying quantities every two hours. The result of this treatment was to allay the excitement in great degree, during which time she had some sleep at intervals, from which she appeared much refreshed. In this case many other hypnotics had been given at various times, but with little benefit, and as the patient was a very large, well-developed woman of good physique, it was decided on this occasion to give the above treatment a trial; and it seemed to afford a considerable measure of success. This is somewhat analogous to the "Bromide Sleep" advocated by Macleod.(2)

Clouston(3) who has made a special study of the action of the bromides, does not seem to believe in administering them alone, for he says: "In acute mania I seldom found the bromide given alone do any good, or indeed, have any perceptible effect. I gave it in all doses up to 120 grains three times a day, and I continued its use in some cases for a few days. But when combined with Tincture of Cannabis Indica, the effects of the mixture were in many cases very remarkable."

The Bromides are certainly admirable for combining with other drugs, such as Chloral, Opium, Hyoscyamus and Belladonna, etc. Here their combination seems to greatly intensify the effects of each/

each, and when the employment of a medicine is being gradually stopped, their judicious administration, frequently renders such withdrawal much less noticeable to the patient.

A combination which is of the greatest benefit in mental disease is that of Chloral Hydrate and Bromide of Potash. In cases of sleeplessness arising, it may be, from acute or chronic mania, delirium tremens, etc., a sleeping draught containing about 15 to 20 grains of Chloral and 40 to 50 grains of Bromide of Potash is frequently most efficacious, and the addition of a little Spirits of Chloroform or Aromatic Spirits of Ammonia, do much towards rendering it not only much more palatable, but of greater value, should there be any asthmatic complication.

In the vast majority of cases of insanity in which I have used Chloral, I have nearly always given the Bromide of Potash or Soda or Ammonium in combination with it. A mixture of the Bromides with Belladonna or perhaps a little Opium is often of great service, or when combined with Hyoscyamus, they form a delightfully sedative mixture, which is of particular service when there is any genito-urinary condition complicating or giving rise to the insomnia. Where the use of the Bromides is going/

going to be long continued, it will be found better to give the Soda salt, as it is less depressing to the heart and better borne by the stomach. Indeed, Bartholow[4] remarks: "When there is much susceptibility to the action of the Bromides, it is generally better to prescribe the Bromide of Sodium." On the other hand, where there is any respiratory affection the Ammonia salt is generally of most value.

Macfarlane[5] recommends the Bromide of Lithium of the U. S. Pharmacopoeia, as the best hypnotic of the bromide salts, as it is richer in Bromine than the others; but he remarks in speaking of their employment: "These drugs have a tendency to lead to an impoverished state of the blood, and this itself leads to insomnia."

If the use of the Bromide salt be long continued it always gives rise to more or less intellectual stupor, and it may even cause Bromism, which I will discuss later on.

Fothergill[6] in speaking of Bromide of Potash says: "Its constant use, however, leads to diminished brain activity and to intellectual lethargy."

Personally, in prescribing these salts, I have always had a special fondness for the Bromide of Potassium, and I cannot say that I have observed any very great drawbacks to its use. It must not, however/

ever, be administered for any length of time, for besides the depressing effect which Potassium exerts on the heart, there is a liability to more or less gastric disturbance being set up. But if it be given in small doses, and not long continued, its sedative action is most beneficial. (7) Fothergill remarks, "Bromide of Potassium has a decidedly sedative effect upon the brain cells; and the cerebral anaemia produced by its administration is rather due to its sedative action upon the cerebral cells by which they attract less blood to themselves than to its effects upon the circulation; though doubtless to some extent it does diminish the activity of the heart."

One of the most important therapeutic uses of the Bromides is the influence they exert in cases of Epilepsy. Indeed, it is in this disease that their influence is perhaps most marked. For they markedly lessen the number of fits and in some cases may stop them altogether. (Except in that variety of Epilepsy known as Petit Mal, where they are frequently of no service whatever.) It is undoubtedly of the greatest importance in prescribing them in this connection, to take pains to ascertain accurately how small a dose of Bromide will suffice, and then keep to that. Certainly there are a large class of/

of epileptics who are so benefited by their judicious use, that they never get the length of the asylum. In cases of Chronic Epilepsy, where their employment has to be long continued, often in large doses, it will frequently be found of the greatest benefit to combine the salts with one another, and now and again administer some Arsenic with them, as this treatment is of the utmost value in lessening the anaemia and acne, which so frequently follow their long-continued use, I have always found the Liquor Arsenicalis or Fowler's Solution, to be the best for this purpose; it may be made up as in the following prescription, which I venture to think will be found a very useful one for this class of case.

R.
Potass: Bromid:
Sod: Bromid: ana ℥i ʃs.
Liquor Arsenical: ℥ ʃs.
Aquae ad: ℥ viii
M.

Sig. A tablespoonful three times a day in water, after meals.

It is a good plan in these very chronic cases of Epilepsy - of which there are always some in every large asylum - to stop the use of the Bromides now and again, for a short period. My own experience is, that there are few, if any, of these cases, which/

of epileptics who are so benefited by their judicious use, that they never get the length of the asylum. In cases of Chronic Epilepsy, where their employment has to be long continued, often in large doses, it will frequently be found of the greatest benefit to combine the salts with one another, and now and again administer some Arsenic with them, as this treatment is of the utmost value in lessening the anaemia and acne, which so frequently follow their long-continued use, I have always found the Liquor Arsenicalis or Fowler's Solution, to be the best for this purpose; it may be made up as in the following prescription, which I venture to think will be found a very useful one for this class of case.

R.
Potass: Bromid:
Sod: Bromid: ana ℥ i ʃs.
Liquor Arsenical: ℥ ʃs.
Aquae ad: ℥ viii
M.

Sig. A tablespoonful three times a day in water, after meals.

It is a good plan in these very chronic cases of Epilepsy - of which there are always some in every large asylum - to stop the use of the Bromides now and again, for a short period. My own experience is, that there are few, if any, of these cases, which/

which will not allow of the employment of the drug being altogether discontinued, or at least lessened in dosage, for a brief period. And I would here just mention, as a point of practical importance, that the "stock Bromide bottle" of the epileptic ward should be thoroughly rinsed out - on these occasions - with some strong acid (I always used pure Hydrochloric myself) and afterwards carefully scalded, so as to prevent the formation of that peculiar fungus looking substance, which is so frequently to be observed floating at the bottom of Bromide bottles, which have not been thoroughly cleansed or changed for some time.

Bromism is a condition which is apt to follow the long-continued use of the Bromides; it consists chiefly in a general loss of tone and vigour throughout the system, accompanied with langour, sleepiness, loss of appetite, fetor, possibly a bromine odour from the breath, weakened tactile sensibility, unsteady gait, dyspnoea on exertion, diminished sexual power, and considerable mental dulness, often accompanied with an acne-like rash, which is chiefly seen about the shoulders and back. This "Bromide Rash" however, is not always evidence of this condition, for I have noticed that it sometimes appears very readily with some people. Brown-Sequard[8] thinks that/

that the cropping out of an "acne-like eruption on the face, neck and shoulders," etc. is an evidence that the Bromide is proving curative, and he even asserts that there is a "positive relation between the intensity of the eruption and the efficacy of the remedy against Epilepsy."

The Bromides, from their power of diminishing reflex action, are powerful anaphrodisiacs and doubtless to this their sedative action is in part due.

Bucknill and Tuke (9) assert that: "Bromide of Potassium given freely and continuously takes away sexual desire and competence; but it produces great weakness and emaciation, and cannot be continued for any length of time."

Before concluding this account of the Bromides, I would just briefly recapitulate the following points, which are of primary importance in their administration: First, when used in sleeplessness arising from overwork and nervous worry, etc.

1. They are best given in combination with some other drug or drugs. In headaches a useful combination is that with Salicylate of Soda, which is highly recommended by Lauder Brunton (10)

2. They should not be used for any length of time.

3. Their use should be withheld in all anaemic conditions.

4. Where/

4. Where there is any gastric disturbance, the Soda salt is to be preferred.

5. They are best given after meals.

6. During their administration, the patient should endeavour to observe a vegetarian diet as far as possible.

Second. When used in Epilepsy.

1. In all cases, endeavour to ascertain how small a dose will suffice.

2. A combination of the salts will often be found to be the most useful.

3. They may be combined with a little Arsenic from time to time in order to guard against Anaemia and Acne.

4. If possible, their administration should be withheld for brief periods.

5. If the Potassium salt be much used, it is often advisable to combine with it a little of the Tincture of Digitalis.

6. The patient should drink plenty of water.

Cannabis Indica: or Indian Hemp is a substance which has been in use in Asiatic countries and in Africa, since unknown times, under the different names of Hashish, Bhang, Ganja, Charas or Churrus; where it is chiefly used as an intoxicant by the natives; who either smoke it alone or mixed with tobacco; while some make it into an intoxicating drink, or eat it as a confection, mixed with sugar or honey.

In the "Arabian Nights" translated by Lane, the drug is mentioned under the name of Beng, as the narcotic used by Haroun Alraschid and others.

Its introduction into Western Medicine dates from the beginning of this century. It consists essentially of the dried flowering or fruiting tops of the female plant of Cannabis Sativa, grown in India, from which the resin has not been removed; and may be described as occurring in compressed, rough, dusky-green masses, consisting of the branched upper parts of the stem, bearing leaves and pistillate flowers or fruits, matted together by a resinous secretion. Its active principle is Cannabin. In 1839 O'Shaughnessy introduced Indian Hemp into this country, and the first extract of it was made for him by Peter Squire(11).

Generally speaking, the drug is a true narcotic like alcohol or Opium, and is sedative, anodyne, hypnotic/

hypnotic, and antispasmodic. When taken internally, should the dose be a sufficiently large one, its effects are very remarkable, for it causes a general feeling of increased pleasure, the person becomes happy and joyous and filled with a sense of mirth, he sees no difficulties before him. This sense of bien-etre rapidly increases, beautiful visions and dreams float before the senses, and he becomes quite unconscious to all his surroundings; after a time this is succeeded by sleep, and on awaking there may be some sickness and depression. Sometimes, its only effect is to cause more or less nausea and sickness.

One of the best descriptions I know, of the effects of Indian Hemp, is that one given by Bayard Taylor in his "Pictures of Palestine" in which he describes the sensations he experienced on taking a dose himself. Dr H. C. Wood of Phíladelphia has also given a most graphic account of his own experiences in this respect.

It is very curious how the sense of perceiving time is utterly lost Bartholow[12] remarks, "Under the influence of Hashish the knowledge of time is lost, such are the number and variety of the images which occupy the mind, that a few minutes, appear to be hours, days or even years."

Those/

Those under its influence can generally be got to answer questions coherently. Their cutaneous sensibility is, however, impaired, and they do not readily respond to a pinch. The stage of excitement which generally lasts about two hours, is much longer than that produced by Opium, but unlike that drug it does not, as a rule affect the appetite or induce constipation.

St. John Moses[13] has recorded a case of considerable interest in which its intoxicating effects were such as to simulate an attack of Mania.

Its two important preparations are the Extract (Dose: ¼ to 1 grain) and the Tincture (Dose: 5 to 15 minims) and it is chiefly with the hypnotic effects of these, that I will concern myself here.

I do not think that Cannabis Indica will be found to be of much value administered alone, but when combined with other drugs, its hypnotic effects are certainly very remarkable.

I have always given it combined with the Bromides or Hyoscyamus and when thus used in Acute or Chronic Mania, it is certainly one of the most valuable drugs which we possess in the treatment of these conditions on account of the extremely sedative action which it induces.

In that form of Mania known as Folie Circulaire,

I/

I have used it with admirable results; administering it in the form of the tincture in 20 minim doses combined with Bromide of Potash in 20 grain doses. In these cases of Acute Mania, characterised by excessive incoherent chattering, it is always most beneficial. Clouston[14] who has written extensively on the virtues of this mixture, remarks: "My experience has been that about 45 grains of the bromide, along with 45 minims of the tincture of Cannabis will have the same sedative effect as a drachm of Laudanum."

I always administered it in one of the two following ways, either as a pill, made from the Extract, along with the Extract of Hyoscyamus, or gave the Tincture added to a solution of Bromide of Potash in water.

This latter method is not a very good one, because, the mixture is of a grass green colour, with an abominable taste; and as the water precipitates the resin in the Cannabis, the medicine always requires to be well shaken before use; further the resin tends to stick to the inside of the bottle, and is almost impossible to shake off; so that the dose cannot always be given with complete accuracy. However notwithstanding these drawbacks, I am old-fashioned enough to use this "green mixture" occasionally, provided the patient can be persuaded to swallow/

low it, its effects are most satisfactory. (The addition of a little mucilage to the solution helps to suspend the resin, and will be found to greatly improve it.)

If the pills are used, I have found it a good plan, to divide them in halves or quarters, before giving them. Because now-a-days, pills are so beautifully coated, that they frequently pass right through the alimentary tract without dissolving at all.

I should mention, that in two cases of Chronic Mania, occurring in women, in which I administered these pills, they seemed to increase the excitement, and I had to discontinue their use; I do not think, however, that this effect is of common occurrence.

It is not yet thoroughly understood how Cannabis Indica acts, or how it is excreted. It is aphrodisiac in its effects, and causes some dilatation of the pupils, but sweating is never great.

It has been found useful in many morbid conditions, more especially in Menorrhagia and Haematuria. Used as an hypnotic, I do not think, that it gives rise to any deleterious effects, indeed Cushny(15) remarks: "The continued abuse of Hashish in the East, sometimes leads to mania and dementia, but does not cause the same disturbance of nutrition as Opium, and/

and the habitual use of small quantities, which is almost universal in some eastern peoples, does not seem detrimental to them."

In Delirium Tremens it is of decided value and does much to cut short an attack; and it is an excellent remedy for Megrim or Sick Headache. Murrell[16] speaking of its use in this affection, says: "It is somewhat surprising, that it is not more frequently employed. The extract, may, be given in doses of from $\frac{1}{3}$ to $\frac{1}{2}$ grain in the form of pill. When the patient suffers constantly from headache, or is liable to an attack on the slightest provocation, a pill may be taken three times a day, for many weeks at a time without the slightest fear of the production of any untoward effect."

The late Sir Russell Reynolds,[17] - from an experience of 30 years - stated that the drug, was of great value in Senile Insomnia marked by great restlessness (Fidgetiness) he gave $\frac{1}{4}$ to $\frac{1}{3}$ of a grain of the extract at bedtime; but regarded the tincture as the best preparation on the whole. Fronmuller[18] who used it purely as an hypnotic administered it in 1000 cases, and found that it succeeded in 530, partly succeeded in 215, and produced little or no effect in 255 instances. Birch[19] reports having found Indian Hemp of great service in curing the "Chloral and Opium/

Opium habits."

Among the non-official remedies of Cannabis Indica, we find four, namely Cannabine, Cannabinol, Cannabin Tannas, and Cannabinon. These have all more or less hypnotic properties, though the two latter are said to be somewhat uncertain in their action, being occasionally inert. Probably this is owing to the difficulty of obtaining the preparations pure. None of them appear to have taken a high place amongst hypnotics. Personally, I cannot speak of their effects, never having employed them. The following is their description and doses:

Cannabine: A syrupy liquid alkaloid. Has been administered in 3 minim doses, as an hypnotic.

Cannabinol: A stable resinous substance. Recommended in ½ grain doses in neuralgia and migraine.

Cannabin Tannas: A yellowish powder. Dose, 5 grains, may be increased to 15 in insomnia.

Cannabinon: A purified resin. Has been given with good results in the sleeplessness of Mania, in doses of ½ to 1½ grains.

Group V. Opium and Hyoscyamus, with their alkaloids.

Opium: Otherwise known as the historic "Gift of God" is a preparation of the juice, obtained by incision from the unripe capsules of Papaver Somniferum or poppy and inspissated by spontaneous evaporation.

Opium is produced in various parts of the world, Turkey, Asia Minor, Persia, and India, and to a slight extent in England, Germany, and the United States. The opium used in this country is for the most part that imported from Asia Minor and is the variety known as Smyrna or Turkey Opium. It occurs in irregular lumps of from ½ to 2 lbs in weight, and when fresh tears with an irregular moist brown surface, and has a strong narcotic odour and taste. Dose ½ to 2 grains.

There are 18 alkaloid preparations in all, and of these Morphine is by far the most important.

I have now to consider one of the most valuable and best known of drugs; and at the same time one that is very ancient. The preparations made from opium and its alkaloids, with all their various therapeutic uses, are far too nemerous to mention here, and for my present purpose, it is unnecessary that I should do so.

The drug is one of very great importance.

From/

From its powerful analgesic action; it is certainly the best pain-killer, which we have; hence its great value in producing sleep.

I fancy, the reader may ask, why then has it not been considered sooner in a dissertation like this? My answer is, that though opium from its analgesic properties is one of the most powerful hypnotics, it cannot, I think be held to take precedence of all other hypnotics, for where its analgesic action is not required I believe that these hypnotics which I have previously considered, are in many cases to be preferred to it.

First, I would consider the general effects of opium, and its action on the various systems of the body.

When the drug is taken into the system, its first effect is to produce a feeling of general well-being; the patient becomes slightly excited, his emotions are pleasurable and his whole horizon appears to be bright and unclouded. The imagination is stimulated, and ideas flow with little effort, various pleasurable fancies float before his mind, which becomes for the time being one of supreme content. After a while, these effects wear off and somnolence ensues, which is more or less heavy, according to the amount of the drug taken. When he wakes/

wakes, there is generally a sense of extreme depression, and there may be more or less nausea, with sickness and headache.

Of course these effects vary considerable according to the temperament of the person, the amount taken, and his or her tolerance of the drug. The confirmed "Opium eater" can frequently take a large amount. I may remind the reader of that "King of Opium eaters", De Quincey(20), who has asserted that he got the length of taking 320 grains per day. In excitable women, small doses may simply increase their excitement, while in others the ingestion of Opium is followed by extreme sickness and general discomfort.

When Opium is taken to stimulate the imagination, its pleasurable effects may be indefinitely prolonged by graduating the dose, etc. Generally speaking, Opium in large doses, affects the whole alimentary tract from the mouth to the anus, checking every secretion, except that of the skin and mammary glands. It is depressant to the circulatory and respiratory systems; large doses of it, causing death by paralysis of the respiratory centre. It is excreted by the kidneys, skin and mucous lining of the stomach.

On the cerebral centres, it produces sleep by depressing and diminishing the functional activity of/

of the cerebral cells, and at the same time causing cerebral anaemia, in which both the arteries and veins are less full.

I believe that the use of Opium, as an hypnotic, is chiefly indicated in these cases where there is pain; in such its prompt analgesic action renders it at once the most effective and valuable hypnotic that we possess. All practitioners of any experience whatever are all more or less familiar with its use, in this respect, and therefore I do not think that I need allude to it further, nor point out the various contra-indications for its use in these cases.

In asylum practice where pain is not the cause of the insomnia, the use of Opium as an hypnotic is, I venture to think, a subject which is open to a considerable amount of discussion. Personally, I do not incline much to its use; the calm and rest which it produces are, I think, too dearly bought, for its after effects are generally accompanied by more or less constitutional disturbance, and frequently with sickness and headache, etc.

If its use is long continued an "Opium habit" is often induced, which must sooner or later be broken, and doing this always entails a more or less considerable amount of suffering to the patient.

Further/

Further, it seems to me that the use of opium causes constipation, loss of appetite and, in many cases, loss of weight. The sleep, which it induces, is always more or less of a "drugged" one, and the patient awaking from it more often experiences a sense of utter discomfort, than a feeling of refreshment.

Of course I know that much will depend on the way the drug is given, the amount of the dose, the preparation used, the condition of the patient, and many other circumstances.

I have frequently used opium in that proprietary preparation which is known as "Nepenthe"; I think that it has a great advantage over all others, in that it does not seem to induce after bad effects, such as sickness and vomiting.

Opium will combine well with the bromides, but if used with chloral it should be given with the utmost caution. I have before alluded to this as a very dangerous combination when speaking of chloral. I think that on account of the depressing effect which opium exerts on the heart that it should be used with caution in Delirium Tremens and Acute Mania. Before going further, I would just consider some of the experiences of others in regard to the use of this drug.

First/

First, let me consider these in favour of it, and in doing this it is indeed very remarkable how much the use of opium and its preparations are recommended in mental disease among the older writers. Some of them certainly seem to have administered it in heroic doses. Valsalva and Morgagni prescribed it, and in more modern times, we read of Cullen giving it in large doses. Esquirol asserts that its use in mania was really due to an accident, a lunatic patient having swallowed an ointment containing 24 grains of the drug, with the result that he was cured. Owing to this circumstance its valuable properties were brought into prominence and many physicians became ardent supporters of the new remedy.

Curiously enough, a case is mentioned by Van Swieten of a maniacal patient who accidentally took a scruple of opium dissolved in vinegar with the gratifying result that he also was cured. After this Swieten employed the drug freely; but never went beyond doses of 15 grains at a time.

Those in favour of opium seem very unanimous, that the cases in which it is to be employed, should be very carefully selected. Macintosh[21] states that injurious effects have followed the administration of opium in insanity from want of discrimination/

tion in the selection of cases for its use, and from the insufficiency of the doses used. In cases where there was great irritability and insomnia, and there was no evidence of permanent organic lesion of the brain, he has seen the best effects result from 80 to 100 drops of Laudanum, given every third hour.

Some have greatly praised the employment of opium in melancholia. Mackenzie(22), who has gone into this subject exhaustively, records many cases which were greatly benefited by its use, and many of them recovered.

Drs Bucknill and Tuke(23) consider that it does good in Delirium Tremens and Mania, and assert that when it is used skilfully and with discrimination that it may be truly called the sheet-anchor of the alienist physician.

On the other hand, Clouston(24) speaking of its use in Melancholia and brain exhaustion, while admitting that it is occasionally of benefit, says: "I am not in favour of opium for many such cases in however small doses, because my experience is that it diminishes the appetite and the patient does not gain, but tends to lose in weight, while a habit and craving are apt to be set up."

I remember administering the tincture of opium in drachm doses daily to a patient who was the subject/

ject of Chronic Mania with exacerbations. The drug acted splendidly for a time; but at the end of three weeks or so an "opium habit" had become established, and it seemed to me that in stopping the medicine I entailed on him as much suffering as he had had when I begun it. Willis objects to opium because it causes constipation and sometimes increases watchfulness.

It seems clearly established that the use of opium in mental disease may be most beneficial in many cases, and worse than useless in others. I think that every case must be judged on its own merits. In these cases where it is used, I would emphasize the importance of having the patients weighed carefully at stated periods; and when any loss of weight is detected, it should at once be discontinued. In all respiratory and renal conditions it is not an hypnotic to be employed at all.

At the present day, we do not hear so much about the use of opium in Insanity, as we did some years ago. Why is this? I think the answer clearly is, that of more recent years newer hypnotics have taken its place.

The three important alkaloidal extracts of opium are, Morphine, Narcein, and Papaverine.

Morphine:/

Morphine:

This alkaloid was isolated by Serturner at the commencement of this century. It occurs in minute colourless shining crystals, bitter in taste, alkaline in reaction. Dose $\frac{1}{10}$ to $\frac{1}{2}$ a grain.

In speaking of the hypnotic uses of Morphia I would regard its employment simply as another method of giving opium and therefore I do not purpose to treat of it at any length, as it would to a great extent be merely a repetition of what I have already said about that drug. It may be administered by the mouth, but it is generally more convenient to give it hypodermically; it has the advantage over opium that it acts more quickly, is more powerful in its action, and as a rule does not cause the same degree of constipation or constitutional disturbance in its after effects. It must always be used with great caution, on account of its highly toxic action. Macfarlane(25) recommends that the tartrate is the best preparation for general use, on account of its solubility, and he advises that it be combined with $\frac{1}{100}$ of a grain of atropine sulphate which checks the tendency to vomit, so often induced by the hypodermic injection of morphine alone, and seems to augment its hypnotic properties.

McIntosh/

McIntosh[26] speaks highly of morphia in an account of a series of cases in which he tried it; he applied it to these patients where restlessness, excitement, and dirty habits occurred at paroxysmal periods.

I have never found much benefit from its use as an hypnotic, unless in those cases where there was pain, - where it is the hypnotic "par excellence" - indeed it is sometimes curiously disappointing. Its free exhibition is more than likely to induce a craving for the drug; and when this state of matters is reached, the sooner its employment is discontinued the better.

Narcein:

Occurs in white silky acicular crystals, with a slightly bitter taste. Dose ½ to 1 grain.

This alkaloid was discovered by Pelletier in 1832. Observers differ considerably regarding its real value as an hypnotic, and it has not as yet come into general use.

Papaverine:

Occurs in white crystalline needles. Dose, 1/12 to ⅓ of a grain.

Discovered by Merck; as yet there seems to be considerable difficulty in getting a pure preparation/

paration of this substance.

I merely mention the two above drugs as they are alkaloidal extracts of opium having hypnotic properties. They are not likely, so far as I am aware, to be of any real value to the alienist physician.

Hyoscyamus or Henbane:

Hyoscyamus Leaves: The sinuated, hairy, dried leaves and flowering tops of hyoscyamus niger, also the fresh leaves and flowers, with their branches - gathered from biennial flowering plants. Hyoscyamus has two active principles, Hyoscine, and Hyoscyamine, and three official preparations, viz.

The Extract (Dose 2 to 8 grains)

The Succus (Dose ½ to 1 drachm)

The Tincture (Dose ½ to 1 drachm)

It also enters into the composition of the Colocynth pill.

In considering this drug, I will speak first of the effects of its preparations, and secondly of its alkaloids.

The general effects of hyoscyamus are mainly sedative, anodyne and hypnotic. When given it produces/

produces delirium, dryness of the mouth, dilatation of the pupils, and sleep. It is mildly diuretic and exerts a most sedative action on the mucous membrane of the genito-urinary tract. Small doses of it have a slightly stimulant effect on the heart, while large doses tend to depress it.

When given with purgatives it does much to correct the griping pains of peristalsis and so renders the action of the bowels much less painful. The fresh juice is generally the best preparation to use.

I do not think that Hyoscyamus can be regarded as a powerful hypnotic, unless it be given in large doses which as a rule are not desirable, but from the general sedative effects which it induces, the drug is of considerable value in asylum practice.

As I have previously indicated, it forms an admirable combination with Cannabis Indica or the Bromides, and given in this manner, its exhibition may be continued for a considerable period in cases of cerebral excitement, particularly chronic mania. In such disorder, I have always employed the tincture administering it in 15 to 20 minim doses, combined with Bromide of Potash, or the extract made up in pill form, with the extract of Cannabis Indica.

In cases of Adolescent Mania which are occasionally complicated with extreme erotic impulse, the drug/

drug will be found of particular value, in such cases, "I have often observed that the patient not unfrequently experiences more or less difficulty in voiding his urine; owing to two causes. Firstly, his extreme nervous agitation - which for a time, may inhibit the stream altogether. Secondly, the congestion produced about the parts, it may be by habits of masturbation.

In such cases I have found that the administration of hyoscyamus with belladonna, is productive of a most soothing effect; and the patient is rendered able to pass water in full stream and without difficulty. I remember a striking case of acute adolescent mania occurring in a boy, where I attempted to pass a gum-elastic catheter to relieve his distended bladder, but owing to his restless condition and extreme excitement, failed. In this case, the timely administration of the above combination proved quite efficacious. Indeed, riper experience has taught me that in such cases, the use of a catheter is not only unnecessary, but may frequently be positively harmful.

Again, in cases of advanced general paralysis of the insane, where retention is of such common occurrence, the use of the catheter may be much diminished by the judicious employment of henbane and/

and belladonna.

I have never found hyoscyamus of any service in directly inducing sleep; its effects are rather simply that of a general sedative, tranquillizing and soothing the patient.

Pereira(27) most aptly observes: "In small and repeated doses, henbane has a calming, soothing, and tranquillizing effect. This is specially observed in persons suffering from great nervous irritability and from a too active condition of the sensorial functions. In such, it frequently causes quietude, with a tendency to sleep."

* * * * * * * * *

"Sometimes, when it fails to cause actual sleep, it proves highly serviceable by producing a calm and tranquil state conducive to the well-doing and comfort of the patient."

Children are said to bear hyoscyamus well in large doses; but in the aged, such are apt to unduly depress the heart.

Hyoscine: This is a syrupy liquid alkaloid, which forms salts, of which the best known are the hydrochlorate and the hydrobromate.

Dose $\frac{1}{200}$ to $\frac{1}{100}$ of a grain.

This/

This drug is one of the most powerful and most dangerous hypnotics in the British Pharmacopoeia. Much has been written about its effects; with some it has proved highly successful, with others, its employment has been followed by disastrous consequences. There still seems to be considerable difficulty in procuring a pure preparation of the substance.

Whitla[28] recommends that Merck's preparation be prescribed, and Binz advises that the first dose should never exceed $\frac{1}{660}$ of a grain. Personally, I think that in the meanwhile, the physician who eschews the use of hyoscine altogether will have no reason to regret his course of action. This may seem to be a somewhat dogmatic statement, but I think that, in the present day, when observers are differing so widely as to its employment, that it is a justifiable one. And, indeed, now-a-days, when there is such a large choice of soporifics, many of which are quite satisfactory, for all practical purposes, it seems unnecessary to run any risks. That there is no risk, I simply deny.

Gordon Sharp[29] who has made a careful investigation of its effects, and who took the greatest care to secure a pure preparation of the substance, concludes his report by saying that: "Hyoscine evidently/

evidently differs little in its action from atropine, and until more is known of its chemistry, pharmacology, and clinical effects, it can hardly in my opinion, be regarded as a safe hypnotic."

However, it is only fair to state that some observers have used it with success, and recommend its employment. Clouston[30] speaks fairly favourably of it, provided the patient is of strong and vigorous general bodily health, and has a sound heart, and Shaw[31] reports having used both alkaloids with success.

It is extraordinarily rapid in its action, no matter how violent the patient may be, he collapses at once after its administration; but, as a rule, its effects do not last beyond 6 or 8 hours, and during this time though inducing quiet, it does not always produce sleep. I think in all cases, where it has been decided to use it, that the physician should be near his patient for some hours after its administration; this is not always easy in private practice, and can only be satisfactorily carried out in hospital and asylum work. It is best given hypodermically.

Hyoscyamine or Hyoscyamia: This is identical with Duboisine. According to Murrell[32] when pure it is in/

in the form of snow-white masses of minute crystals, soluble both in spirit and water. It is often mixed with hyoscine, when it is known as amorphous hyoscyamine, which is a dark brown substance looking like an extract and having a strong disagreeable odour.

Dose, $\frac{1}{200}$ to $\frac{1}{100}$ of a grain of the sulphate hypodermically.

There seems to be great difficulty in obtaining this alkaloid pure, and it is probably on this account that all observers appear to differ regarding its effects.

On the whole, it does not seem to be a safe hypnotic by any means. Indeed, it is much more uncertain in its effects than hyoscine. And until more is known of it, I do not think it is to be recommended. Clouston[33] characterises it as "an altogether dangerous drug." Personally, I have had no experience of it.

Group VI. Miscellaneous.

"Good wine is a good familiar creature, if it be well used." (Othello)

Alcohol:

It/

It is unnecessary in a work of this nature, that I should write at any great length on the action and many therapeutic uses of alcohol. The drug is one whose general uses and properties are altogether too well known to want any description on my part.

In writing, however, on the subject of hypnotics, not to mention alcohol would be to render the list incomplete. For such a drug, when used in suitable cases and administered by the experienced, combines at once in its many properties, not only an hypnotic, but a food, and a powerful stimulant.

Alcohol as an hypnotic, may be used in two ways: Firstly, it may be administered alone. Secondly, it may be used as a vehicle for the administration of other remedies.

Considering the first of these methods: there is no doubt that to those unaccustomed to its habitual use, a glass of whisky, especially if it be taken warm, before retiring to rest, will frequently afford a good night's sleep, its action being at once to promote a feeling of comfort, warmth and general well-being, which soon brings on somnolence. But before administering alcohol for the purpose of inducing sleep the important question must always be considered - Is it likely to set up a habit? If this question can be satisfactorily answered in the/

the negative, we are then in a position to consider those cases, in which its administration for hypnotic purposes is justifiable and its mode of action in them.

In the young, where there is general weakness and restlessness, as in conditions of fever, the convalescence from acute diseases, and other lesser forms of weakness, giving rise to wakefulness at night, we find that the administration of a little alcohol, especially if it be taken hot at bedtime, will act on the cerebrum as a direct hypnotic, its further action being to stimulate the heart, and cause a dilatation of the arterioles, especially those near the surface of the body, and so a feeling of warmth is produced, gentle diaphoresis is induced, and should the patient have had a warm bath prior to its administration, the perspiration is greatly increased. Hence its salutary effect in overcoming a chill.

Alcohol at first quickens and then slows respiration; but in small doses its action here is slight, and may be disregarded for the present. Oxidation within the system is retarded and the excretion of urea is lessened. On the urinary system its action is to a slight degree diuretic, alcohol in the form of Gin being markedly so, while its/

its astringent and analgesic actions are well seen in Diarrhoea and Dysmenorrhoea. In administering alcohol to the aged and those weakened by disease, its marked stimulant action - particularly on the heart - render it a very valuable drug. In large doses it is a true narcotic, but differing from other narcotics in having a longer period of excitement and well-being. The phenomena in drunkeness are too well-known to require any description. In toxic doses it causes death by paralyzing the respiratory or cardiac centres.

By lessening the oxidation within the system, it reduces temperature and many consider this to be one of the chief indications for its administration. In small doses, it is used up as a food, like sugar, producing vital energy and heat.

Binz[34] states that alcohol, with the exception of a minute fraction, is completely oxidized in the organism, acting as a fuel. The principal result being a great saving of albumen. Should there be any food in the stomach, the presence of a small quantity of alcohol will greatly aid digestion.

These remarks, however, apply to such cases where the patients are unaccustomed to its habitual use. To those who are habituated to it, its ingestion will not cause such a beneficial reaction, and/

and in those who take it to excess, its beneficial effects are altogether lost and its action becomes simply that of a poison.

All these are but commonplace remarks, and their truth has doubtless been demonstrated many a time to those observant of its effects. I think, however, they clearly illustrate that, in very many conditions, the administration of a small quantity of alcohol as a soporific, is frequently a most valuable remedy.

I now pass on to consider these cases where alcohol is used as a vehicle for the administration of other drugs. The addition of a small quantity of brandy or whisky will nearly always render a sleeping-draught much more palatable, nay more, but it is also the means of stimulating the gastric, and intestinal glands, so that its absorption into the system is the more readily brought about, and its soporific effects produced sooner. Again, the depressing effects of a drug, may be quite antagonized or overcome by the addition of alcohol. For example, some brandy or whisky added to a chloral and bromide mixture renders it much less depressing in its effects.

On the other hand, I now enter on the consideration of some of the contra-indications for its use. In/

In all these cases where its administration might lead to a habit, or render worse, such habit already formed, of course its use must be avoided. And it is well not to employ it unnecessarily as a means of disguising the taste of other remedies, and so rendering such more palatable.

In the treatment of Delirium Tremens, the insomnia and restlessness is often most distressing: and when the whole system is already low and the heart weak, it becomes a grave question if one should not have recourse to the exhibition of alcohol, in small doses, for a short period; just to tide over what may frequently be a dangerous crisis.

To those who have treated many cases of Delirium Tremens it must many a time have been quite apparent that to give a little alcohol was to produce a wonderfully calming effect, at least for a brief period. I remember a very striking case, where a patient who had come voluntarily to the asylum, suffering from hallucinations of hearing, brought on by intemperance, told me that the voices he heard telling him he had to die, etc., would always go away if he yielded to the temptation and took a little drink, and that latterly he had just been drinking to keep the voices away. I think, however, in all these cases it is certainly best to withdraw the alcohol at once and for/

for good. There is no doubt that the suffering is in many cases very severe, but in such as will stand it, it is best in the end. And personally I think there are few cases where this treatment cannot be carried out.

In pneumonia, before the "crisis" there are many who advocate the administration of cardiac stimulants such as digitalis, strophanthus, alcohol, etc., to guard against heart failure. I doubt very much, however, if this teaching is quite sound. Dr Keith[35] long ago pointed out that in pneumonia, the chief endeavour should be to give the inflamed lung rest, and that to administer stimulants in any form was to stimulate the heart and drive more blood through the already weakened lung; and thus the inflammation was increased on account of the lungs being over-charged with blood; and matters were made worse than they were before. On these grounds Keith held that stimulants should only be given as a last resort, when cardiac failure threatened. I think that this is specially true as regards the employment of alcohol in this disease; and I believe it to be best in the great majority of cases, so far as the administration of alcohol is concerned, to withhold it as long as is possible, and then only give it as a last resort. There is

one/

one other reason why I think it should be withheld in pneumonia and that is this, that its exhibition frequently brings on delirium, or causes such to become worse if it is already present. I believe this to be partly if not entirely owing to the fact that, in these cases, a very small amount will simply have the effect of causing intoxication, owing to the weakened condition that the patient is already in. I fear, however, that to enter further on this subject would be to digress from the hypnotic action of the drug.

In all cases where there is kidney mischief, or manifestations of hysteria, and hypnotics are likely to be required, alcohol should not be given. It should also be withheld in all genito-urinary conditions complicated with stricture, as its effects in these cases is to increase the congestion of the part and make the stricture worse.

I do not think that alcohol should ever be regarded in the light of a simple and harmless remedy for insomnia; it is at all times a remedy which either for its hypnotic effects or anything else, should always be prescribed with the greatest caution, and if the medical attendant should entertain the slightest misgivings as to its employment, I think he should allow himself to be guided by the motto "When in doubt, abstain."

Urethane: ($C_3H_7NO_2$)

The ethylic ester of carbaminic acid. Prepared by the action of nitrate of urea on ethyl-alcohol. Occurs in colourless prismatic crystals, with a peculiar cooling taste, free from odour.
Solubility, 1 in 2 of water.
Dose, 15 to 30 grains, 45 to 60 grains have been given.

This drug is not official. It is a pure hypnotic, having no anodyne properties. Attention was first called to it by Schmiedeberg[36] and since then it has been physiologically investigated by Jacksch[37] and Von Anrep[38]. It is a weak hypnotic, somewhat uncertain in its action, but having no dangerous after effects. In favourable conditions it will usually procure about five or more hours sleep, when given at bedtime. And it sometimes acts promptly when other drugs are contraindicated.

Von Jacksch[39] administered it in a cardiac case where chloral and morphia could not be given. And again in a case of painful thoracic aneurism. In both of these it gave very good results. Altogether, he used it 110 times in twenty different cases and was highly satisfied with the results obtained.

Sieveking[40] and Manifold after giving it an extensive/

extensive trial in hospital practice where the patients were closely observed, report favourably on its hypnotic properties. And Saundby[41] recommends it in two grain doses, for the sleeplessness of cardiac disease, where there is dilatation. Opinions differ considerably, however, with regard to the use of urethane, and the drug does not seem to have come into very extensive use, notwithstanding the fact that its price is much lower than formerly.

Whitla[42] says he has been invariably disappointed with it, and that it is of little good except in the case of children. On the other hand, Kraepelin[43] and Myrtle[44] report very favourably on its use as an hypnotic, the former having administered it in about 200 cases of insanity. He observed no bad effects at any time and speaks of it as a genuine hypnotic, but of no value in excitement or delirium tremens, though useful in melancholia, and chiefly indicated in exhausting diseases where there is feverishness and lowered nutrition. While the latter, who has used it extensively in general practice for sleeplessness, and general restlessness, in Neuralgia and Catarrh and in gouty and rheumatic conditions, concludes by recommending it strongly.

Urethane does not injuriously affect the secretions and does not cause constipation; it is more easily/

easily taken than either paraldehyde or amylene hydrate, though its therapeutic action is much inferior to them both. I gave the drug an extensive trial lasting over two months in many forms of mental disease, complicated with insomnia. I tried both small and large doses, but my experience is that it is of no practical use in insanity. Probably in the lesser forms of insomnia arising purely from functional causes, its exhibition may often be tried with advantage.

Somnal $(C_{17}H_{12}Cl_3O_3N)$

Or Ethylated chloral-urethane, is a compound of chloral, alcohol, and urethane. Occurring as a colourless liquid, with a faint chloral-like odour. Dose, 30 to 40 minims.

This substance has been introduced by Radlauer (45) who claims for it that there are no unpleasant after-effects, nor interference with the digestive, circulatory, or respiratory organs, and as a rule it acts in about half an hour, affording 6 to 8 hours sleep, having all the advantages of chloral, without any of its disadvantages. He advises that it should be prescribed in half drachm doses, mixed with water and syrup.

Myers/

Myers[46] speaks highly of it, saying it is valuable in sleeplessness of nervous origin, and in convalescence from acute diseases; but is less reliable in pain, and though sedative in whooping-cough, asthma and chorea, etc., it has no influence over inflammatory conditions. Khmielefski[47] after using it in asylum practice, found that in the few cases in which it was given, that it was a valuable and reliable drug. It produced sleep indistinguishable from natural sleep; and in some respects seemed to possess advantages over trional, and chloralose; but he says it is contra-indicated if there is any gastro-intestinal disturbance present, as it tends to increase this.

Somnal is not a powerful hypnotic and is one of modern introduction. Though at first strongly advocated by its supporters, it is not now much heard of. It should be exhibited with caution. There do not seem to be very many reports of its use, and it is difficult in our present state of knowledge to form a just estimate of its value; but I venture to think it is doubtful if it will ever become very popular, as an hypnotic in asylum practice.

Hypnone ($C_6H_5CO\ CH_3$)

Or aceto-phenone, is prepared by the action of chloride of benzoyl on zinc methyl; or by distilling together a mixture of benzoate and acetate of calcium.

Occurs as a colourless mobile liquid having an odour not unlike Oil of Bitter Almonds or Cherry-Laurel water. Insoluble in water. Soluble in 1 in 90 of Glycerine. Dose 2 to 8 minims.

This substance was accorded soporific properties in 1885 by Dujardin-Beaumetz and since then his discovery has been fully confirmed by Constantine Paul[48] and Huchard. According to its discoverer[49] it will cause sleep in doses of three minims, and in alcoholic subjects he thinks its action is superior to paraldehyde or chloral hydrate.

Hypnone requires to be well-diluted, as otherwise it is very irritant to the mucous menbranes. It is at all times very nauseous and the dose requires to be increased. It is said to cause about five hours sleep as a rule. Altogether it is not a drug to be recommended and even Dujardin-Beaumetz himself admits that its effects are not always constant. Whitla[50] calls it an uncertain and dangerous drug, and says, there cannot be a doubt but that it will rapidly cease to be used as a sleep-producer/

producer. If administered it is best given in capsules, or diluted with glycerine or almond oil and administered at bedtime.

Methylal ($C_3H_8O_2$)

Or Methylene-di-methyl-ether, is a colourless volatile liquid prepared by distilling Methylic alcohol with sulphuric acid in the presence of manganese peroxide. It is soluble in water, alcohol, and oil.

Dose, 30 to 120 minims, given in water. This substance was prepared chemically by Malaguti[51] in 1839; and suggested as a medicine in 1887 by M. Personali, being first put to therapeutic uses in this country by Richardson.

Tsisvitski[52], who has studied its physiological effects on frogs, dogs, and other animals, finds that:

1. It diminishes the irritability of the brain.
2. It only diminishes reflexes in large doses.
3. Does not cause sleep in dogs.
4. Quickens heart, by acting on accelerator centre.
5. Raises blood-pressure at first, afterwards diminishing it.
6. Increases the rapidity of the respirations.
7. Has no effects on the temperature of the body.

Methylal has been used as an hypnotic in insomnia, and is claimed to be the best hypnotic in Delirium Tremens. It seems as yet to be comparatively unknown, and may be regarded as being still on its trial. It is said, to cause four or five hours sleep, but that toleration of the drug is soon established; and the dose must then be increased, or its administration discontinued altogether for a few days. Mixed with ether and used as an anaesthetic, it has given favourable results.

Hypnal.

Or Monochloralantipyrine, is a crystalline compound, obtained by the mutual reaction of Chloral and Antipyrine.

Bardet(53) states that Hypnal consists of about 45 per cent of Chloral and 55 per cent of Antipyrine. There are several combinations of this substance, and one at least, is inactive. Hertz(54) reports, that the most efficient hypnotic is Filehne's Hypnal, which acts usually within twenty to thirty minutes.

It is almost tasteless. Dose, 15 to 30 grains.

The therapeutic action of this drug, is similiar to that of its constituents. That is to say, it possesses slight analgesic properties, and administered in large doses, produces some degree of muscular/

muscular relaxation, with dilatation of the arterioles and a depressant action on the heart. Whitla[55] states that it is an effective hypnotic in 20 grain doses in ordinary cases of insomnia. Hypnal is contra-indicated in all cardiac affections. Owing to its analgesic action, it is sometimes efficacious when other drugs would fail.

Chloral and Antipyrine must at all times be administered with care; and for that reason, this drug would seem to me, to be rather a dangerous combination, and one that is not likely to become a favourite in the treatment of insomnia.

Piscidia.

This substance is also known as Jamaica dogwood, and is the bark of the root of Piscidia Erythrina. The shrub is a native of South America and the West Indies, and has one preparation, viz. Extractum Piscidiae Liquidum:- One fluid ounce is equal to one ounce of the root "Squire" (56) Dose, 30 to 120 minims.

Piscidin is a dry alcoholic extract, and may be given in doses of ½ grain. Piscidia was introduced as a substitute for opium, which it somewhat resembles; only on the whole it is more hypnotic and less anodyne in its effects. The drug has been chiefly/

chiefly used in America, and it would appear that it is somewhat uncertain in its action and cannot always be relied upon as an hypnotic. It should be administered cautiously at first, as it reacts differently with different people. Altogether it does not seem to have realised the high expectations of its supporters.

Pellotine and Propione have both hypnotic properties. The former is the name given to an alkaloid obtained from the mescal button, i.e. one of the tops of Anhalonium Lewinii, a plant of the cactus order. The latter has been successfully used by Giovanni in mania, and other forms of Cerebral excitement. It is a limpid liquid otherwise known as Di-ethyl-ketone.

Neither appear to be of any practical use in the present day, and I only mention them to dismiss them.

Lastly, there are a considerable number of hypnotics - some of them of comparatively little importance - the consideration of which, need not detain us long.

Antipyrine and Phenacetin though really coming under the category of analgesics, have hypnotic effects/

fects of no mean power. They are especially indicated in feverish conditions, when there is pain. The former is said to be occasionally apt to cause toxic phenomena; and accordingly must be used with care. The latter is a perfectly safe drug, and is always most beneficial in its effects. Indeed my own opinion of Phenacetin is, that it is a much more valuable hypnotic than is generally supposed. I have used it in all sorts and conditions of cases, and always with more or less beneficial results.

Lactophenin somewhat resembles it, and is a mild and useful hypnotic.

Chloroform, though really coming under the head of anaesthetics, is a drug whose hypnotic properties I would briefly refer to here. Simply to say that I have administered it with marked benefit on several occasions; in order to stop those terrible outbursts of maniacal violence, which are not uncommon amongst the more dangerous class of epileptics. In such cases I have always found its administration to be quite safe, and though this may appear to the lay members of the profession, to be rather strong measures to take, to bring about sleep, I really think that it is often best in these cases to get the patient rapidly under its influence rather than allow/

allow him to carry on a protracted struggle with his attendants, which, however careful they may be, not infrequently end in the patient injuring both himself and others. In such cases - as I speak of - the chloroform-narcosis stops the violence at once, and when the patient wakes, he has generally forgotten all about it, and is in a more tractable mood.

Duboisine is an alkaloid identical with hyoscine or hyoscyamine in its physiological effects. Some have reported favourably on its employment, but I do not think it will ever come much into prominence. It appears to have been more used on the Continent than in this country. And toxic symptoms have often been noted as following its exhibition.

The Monobromide of Camphor is a fairly useful and mild hypnotic.

Macfarlane[57] recommends it in four grain doses as being often helpful in the insomnia which may accompany pregnancy.

Lupulus (Hops) and Sumbul are both substances possessing mild hypnotic properties. Their tinctures administered in combination with other drugs are often useful adjuvants to the sleeping-draught. Bradbury[58] strongly advocates a mixture consisting of Bromide, tincture of sumbul, and tincture of hop in/

in camphor water, as being a combination of much value, especially in the flushing heats which not uncommonly accompany the climacteric period.

Lupulus, in the form of a hop pillow is thought by some to possess peculiarly soporific virtues.

Musk is credited with having mild hypnotic properties. But it is doubtful if it is really of any practical value; and its expense certainly renders its employment quite prohibitive.

Boldo-Glucin which is a glucoside isolated from the leaves of the boldo tree, and its alkaloid Boldin have both been given as hypnotics, with a certain degree of success in some cases.

Chamomile Flowers made up in a muslin bag and wrung out of very hot water, will be found to be a most soothing application in cases of painful gum-boil and swelled face. Their perfume seems to possess peculiarly soporific properties.

The administration of Dovers Powder, especially in feverish conditions, does much to bring about sleep.

In the insomnia of heart disease, Digitalis is often the best hypnotic administered throughout the day.

Turpentine, administered in capsules is sometimes very useful. It seems to procure rest by checking the excessive acid fermentation which is so prone to occur in the alimentary canal of those troubled with Dyspepsia.

Sometimes a glass of water, or better still, milk, especially if it be taken hot, before retiring to rest is often productive of sleep.

It must not be forgotten, that insomnia often arises, simply from constipation, and the administration of a smart purge will often set matters right again. The sedative effect following a dose of Castor or Croton oil is most marked.

Lettuces are said to possess sleep-producing properties, and some recommend a lettuce salad, washed down by a draught of beer as being a delightfully soporific supper.

* * * * * * * * *

EDINBURGH

1900.

REFERENCES.

Chapter I.

(1) Virgil: AEnied, Book IV. (Line 522 to 528)

"Night came, and weary animals of earth were culling peaceful sleep, woods and wild waves were hushed, then stars are rolling in their zenith course, then every plain is still, beasts and many-coloured birds - such as frequent the wide limpid lakes, and ragged brambles of the field, lulled in sleep beneath the stilly night, lay, resting their cares and toil forgetting hearts."

(2) "New York Medical Journal", Oct. 7th, 1899.

(3) Shakespeare: King Henry IV. Part II. Act III. Scene I.

(4) Lancet. 16th October, 1897.

* * * * * * * * *

Chapter II.

(1) Mental Diseases (Clouston), p.708.

(2) British Medical Journal, Vol. I. 1889. p.119.

(3) Textbook of Mental Diseases,(Bevan Lewis) p.477.

(4) Materia Medica and Therapeutics,(Whitla) 7th Ed.

(5) British Medical Journal, July 1891.

(6) Mental Diseases (Clouston) p.708.

(7)/

(7) Practitioner, Vol. II. 1888, P.339.

(8) A System of Medicine (Allbutt).

(9) British Medical Journal, Vol. I. 1889, P.119.

(10) Practitioner, Vol. I. 1887, P.35.

(11) Therapeutics (Wood) P.193.

(12) Lancet, Vol. I. 1886, P.127.

(13) British Medical Journal, Epitome, Vol. II. 1894, P.64.

(14) Medical Annual 1893, P.216.

(15) "Croonian Lectures", July 1899.

(16) Medical Annual 1891.

(17) Materia Medica and Therapeutics, (Whitla).

(18) Year-book of Treatment 1894, P.73.

(19) Medical Annual 1894, P.426.

(20) Materia Medica and Therapeutics, (Whitla).

(21) Mental Diseases, (Clouston), P.246.

(22) Glasgow Medical Journal, 1895.

(23) The Action of Medicines, (Lauder-Brunton) P.181.

(24)/

(24) Mental Diseases, (Clouston), P.710.

(25) Glasgow Medical Journal, December, 1895.

(26) British Medical Journal, September, 1898.

(27) Berlin Klin. Woch, September 26th, 1898.

(28) British Medical Journal, November, 1899.

(29) Berliner Klin. Wochenschrift, No.7, 1889.

(30) Materia Medica and Therapeutics, (Whitla).

(31) Practitioner, Vol.I., 1889.

(32) Therap. Monatshefte, August 1888.

(33) Berliner Medical Wochenschr, June 18th 1888.

(34) British Medical Journal, 1899.

(35) Ibid, Vol.II. 1895, Epitome, P.43.

(36) Medical Annual, 1899.

(37) Materia Medica and Therapeutics, (Whitla).

(38) Internationale Klinische Rundschau, No. 45, 1894.

(39) British Medical Journal, 1895, Vol.I, P.153.

(40) Lancet, Vol.II. 1894, P.212.

(41)/

(41) Practitioner, Vol.I. 1895, P.87.

(42) British Medical Journal, November 1899.

(43) Materia Medica and Therapeutics, (Whitla), P.602.

(44) Mental Diseases, (Clouston), P,177.

(45) Worcester Report for 1872.

(46) Mental Diseases, (Clouston) P.706.

(47) Materia Medica and Therapeutics, (Whitla).

(48) Psychological Medicine (Bucknill and Tuke) P.721.

(49) Mental Diseases, (Clouston) P.490.

(50) Wood's Therapeutics, P.183.

(51) Mental Diseases, (Clouston) P.177.

(52) Materia Medica and Therapeutics, (Whitla) P.359.

(53) Ibid.

(54) Psychological Medicine (Bucknill and Tuke) P.721.

(55) Pharmacology (Lauder - Brunton).

(56) Lancet, Vol.II. 1878, P.83.

(57) Wood's Therapeutics, P.206.

(58)/

(58) Materia Medica and Therapeutics, (Whitla) P.343.

(59) British Medical Journal, 1899, P.74.

(60) Ibid, Vol.I. 1879, P.667.

(61) Wood's Therapeutics, P.206.

(62) Handbook of Therapeutics, (Ringer).

(63) Pharmacology, Materia Medica and Therapeutics, (Lauder - Brunton), P.794.

(64) Lancet, Vol.II. 1889, P.849.

(65) Dictionary of Treatment, (Whitla), P.454.

(66) Lancet, Vol.I. 1890, P.546.

(67) Textbook of Mental Diseases, (Bevan Lewis) P.477.

(68) Medical Annual, 1893.

(69) Lancet, Vol.I. 1890, P.339.

(70) British Medical Journal, Vol.I. 1890, P.1151.

(71) Materia Medica and Therapeutics, (Whitla) P.519.

(72) Lancet, Vol.I. 1895, P.1307.

(73) Ibid, Vol.II. 1893, P.1486.

(74) British Medical Journal, Epitome, Vol.II. 1894, P.60.

(75)/

(75) Ibid, Vol.I. 1895, P.104.

(76) Ibid, Vol.II. 1893, P.91.

(77) Ibid, Vol.I. 1894, P.39.

(78) Ibid, Vol.II. 1894, P.52.

* * * * * * * * *

Chapter III.

(1) Materia Medica and Therapeutics, (Bartholow), P.543.

(2) British Medical Journal, Vol.I. 1900, P.134.

(3) Medical Chirurg Review, XLVII., 1871.

(4) Materia Medica and Therapeutics, (Bartholow), P.546.

(5) Insomnia and its Therapeutics, (A. W. Macfarlane) P.88.

(6) Practitioner, XVI. 1876, P.114.

(7) Ibid.

(8) Materia Medica and Therapeutics, (Bartholow), P.545.

(9) Psychological Medicine, (Bucknill and Tuke), P.760.

(10/

(10) Practitioner, LII. P.101.

(11) Squire's Companion to the British Pharmacop. (17th Ed.) P.179.

(12) Materia Medica and Therapeutics, (Bartholow), P.464.

(13) Thesis on Dysentery, (St. John Moses) 1900, P.225.

(14) Medico-Chirurg Review, XLVI. 1870.

(15) Textbook of Pharmacology, (Cushny).

(16) A Manual of Pharmacology and Therapeutics (Murrell) P.464.

(17) Tuke's Dictionary of Psychological Medicine (Art: "Sedatives".)

(18) Handbook of Therapeutics, (Ringer and Sainsbury) P.583.

(19) Lancet, Vol.I. 1889, P.625.

(20) Confessions of an English Opium-eater(De Quincey) P.220.

(21) Practice of Physic, (Macintosh).

(22) Opium in Melancholia - Thesis - (W.H.MacKenzie) 1898.

(23) Psychological Medicine (Bucknill and Tuke) P.707.

(24) Mental Diseases, (Clouston), P.706.

(25)/

(25) Insomnia and its Therapeutics, (A.W.Macfarlane) P.93.

(26) Journal of Mental Science, P.407, October, 1861.

(27) Materia Medica and Therapeutics, (Pereira) P.541, et seq.

(28) Materia Medica and Therapeutics, (Whitla) P.400.

(29) Practitioner, January, 1894, P.22.

(30) Mental Diseases (Clouston)

(31) Medical Annual, 1895, P.332.

(32) A Manual of Pharmacology and Therapeutics, (Murrell) P.444.

(33) Mental Diseases, (Clouston) P.716.

(34) Materia Medica and Therapeutics, (Whitla), P.320.

(35) "Plea for a simpler life". (Keith)

(36) Archiv. for Exper. Path. Pharm. XX. 210.

(37) Wien. Med. Blatter, 1885.

(38) London Medical Record, December 15th, 1886.

(39) British Medical Journal, Vol.II. 1885, P.611.

(40) Ibid, Vol.II. 1886, P.108.

(41)/

(41) Ibid, Vol. I. 1886, P. 354.

(42) Materia Medica and Therapeutics, (Whitla) P.608.

(43) British Medical Journal, Vol. II. 1886, P.468.

(44) Ibid, Vol. I. 1886, P.343.

(45) Lancet, Vol. II. 1889, P.1024.

(46) "New York Medical Review", March 12th 1892.

(47) Lancet, Vol. I. 1895, P.1024.

(48) British Medical Journal, Vol. I. 1886, P.354.

(49) Ibid, Vol. II. 1889, P.969.

(50) Materia Medica and Therapeutics, (Whitla) P.550.

(51) Wood's Therapeutics, P.215.

(52) Medical Annual, 1891.

(53) Ibid, P. 35.

(54) Year-book of Treatment, 1894.

(55) Materia Medica and Therapeutics, (Whitla) P.550.

(56) Squire's Companion to the British Pharmacopoeia, P.489.

(57) Insomnia and its Therapeutics, (A.W.Macfarlane) P.339.

(58) System of Medicine (Allbutt), (Art: Sleeplessness)